Toxicological investigation of nanoparticles - effects on human cells

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Introduction

Ambient air particles have recently received much interest because of increasing epidemiological and experimental evidence for their effects on health. Which characteristics of particulate pollution are responsible for the health effects are not clear yet. But several epidemiological studies have indicated that the fine and ultrafine particles are more responsible for the respiratory effects than the coarse particles.

The aim of the present study was the establishment of an in vitro test system to reveal the potential risk to human health of nanoparticles at the workplace. The essential advantage of in vitro investigations is to be non-invasive, the employees don't have to be bothered and the work routine doesn't have to be intercepted.

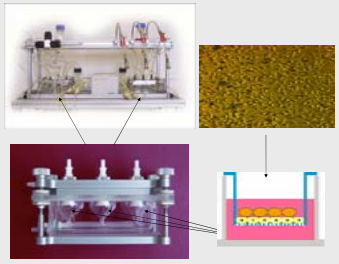
Methods

At a shooting stand test cells on Transwell® inserts were exposed to the workplace atmosphere (E) or to particle filtered air (C) for 1 to 3 hrs using a CULTEX® System. Cells left in the incubator served as additional control (IC).

2 types of co-cultures were tested: In type 1 differentiated macrophages (U-937) were exposed and post-incubated with human lung epithelial cells (A-549). In type 2 differentiated macrophages were seeded on human lung epithelial cells and the co-culture was exposed.

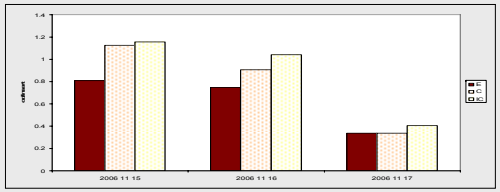
Endpoints for particle exposure:

- cell viability (WST-1 Assay)
- oxidative stress (DHR-Assay)
- pro-inflammatory cytokines (BD™ CBA-Assay): IL-1 ß, IL-6, IL-8, IL-10, IL-12 und TNF-α

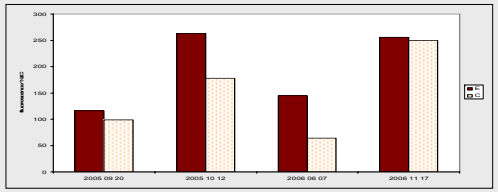


Results I

WST-1 Assay: Cell viability testing showed a negative effect at high exposure.

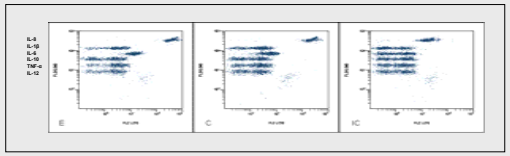


DHR-Assay: In cells exposed to the workplace atmosphere, an increased oxidative burst was detected compared to cells exposed to particle filtered air.

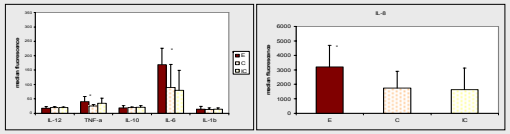


Results II

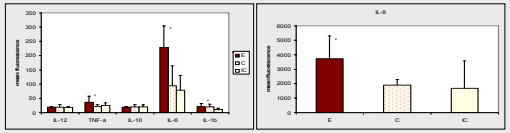
CBA-Assay: Exposure of co-cultures resulted in significantly enhanced cytokine levels. Exposing type 1 co-cultures, TNF-α, IL-6 and IL-8, exposing type 2 co-cultures, TNF-α, IL-6, IL-1ß and IL-8 were significantly enhanced compared to C (*, p<0.05).



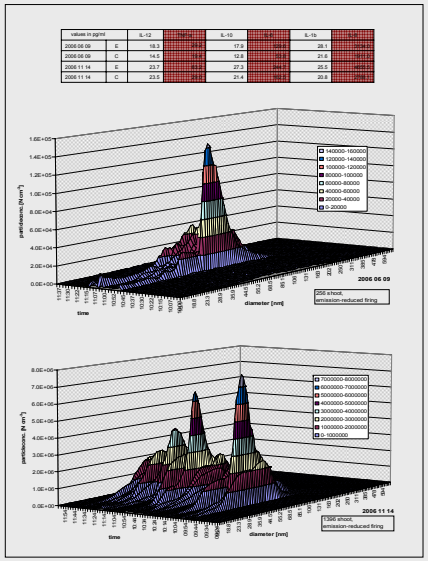
Co-culture type 1:



Co-culture type 2:



Correlation of biological parameters with exposure rates: There was a correlation between high exposure and enhanced cytokine levels.



Conclusion

We could show that our in vitro exposure system is very well adapted for the assessment of adverse effects of nanoparticles at the workplace. Our results indicate that nanoparticles involve an occupational risk and further experiments will be performed to analyse additional endpoints.

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