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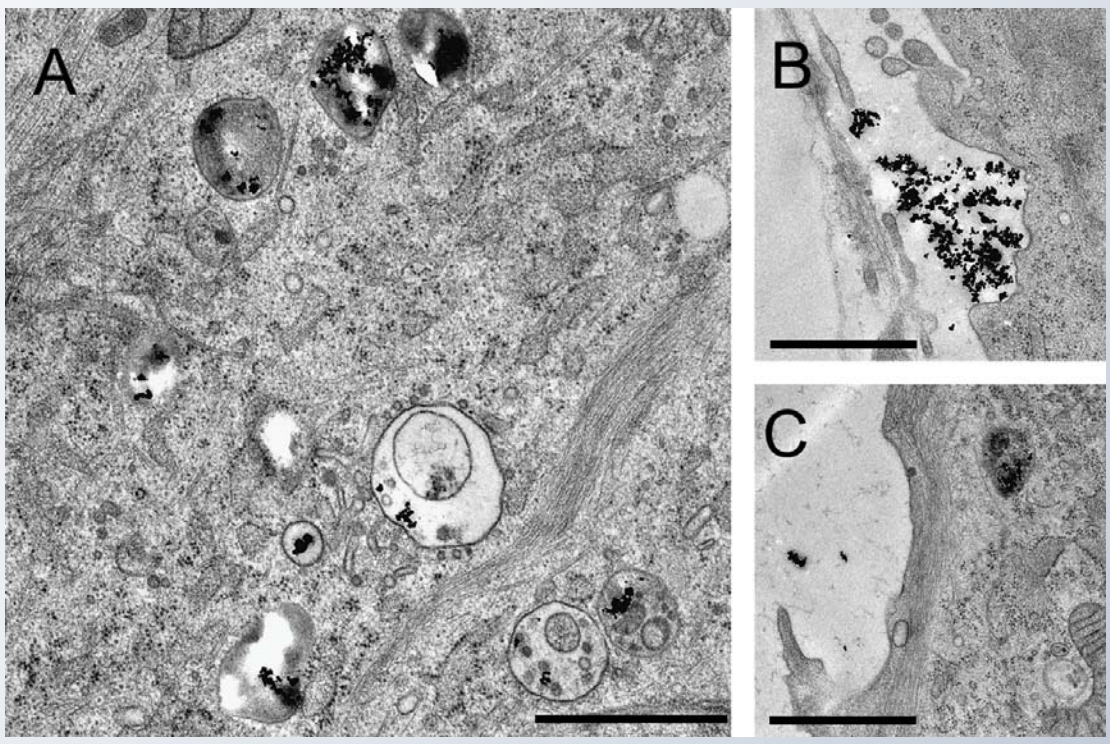
Cytotoxicity of Oxide Nanoparticles: Comparison to Asbestos, Silica, and the Effect of Particle Solubility

Human lung fibroblast exposed to ceria nanoparticles



Bar sizes = 1.5 µm

Exposure of human lung fibroblast cells to ceria nanoparticles of 20 to 50 nm diameter results in the uptake of agglomerates. Vesicles inside a fibroblast cell with ceria agglomerates. The high atomic mass of ceria and resulting contrast make the particles visible as dark spots. Uptake of ceria nano-particles in human lung fibroblasts is shown by transmission electron micrographs.

Motivation

Early indicators for nanoparticle derived adverse health effects may be based on a comparison of the cytotoxicity of nanomaterials to existing toxicological data on commodity chemicals.

We have therefore evaluated two standard cell lines, a human mesothelioma and a rodent fibroblast cell line for *in vitro* cytotoxicity tests using seven industrially important nanoparticles.

The inclusion of highly toxic crocidolite asbestos and non-toxic silica particles allows a comparison of the effect of a series of nanomaterials referring to well-established references.

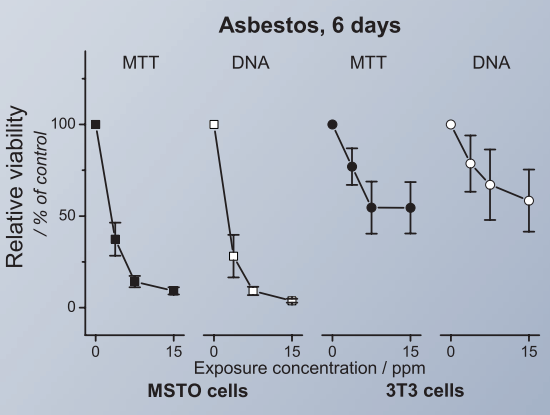
MTT – Assay

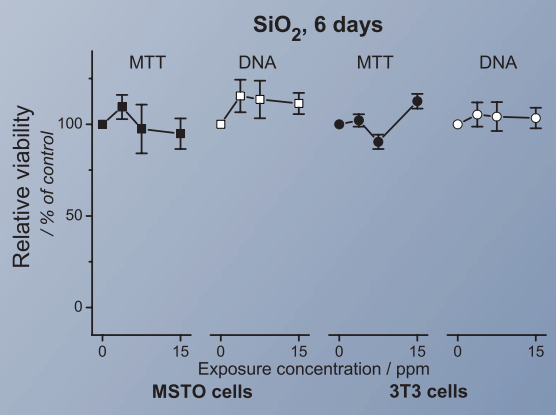
The MTT assay measures the activity of mitochondrial enzymes and can be used as a measure for the overall metabolic activity of a cell culture

DNA – Hoechst – Assay

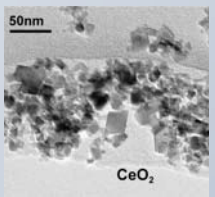
The DNA Assay measures the total amount of DNA in a cell culture. This can be correlated to the amount of cells and allows to detect changes in cell proliferation and growth rate.

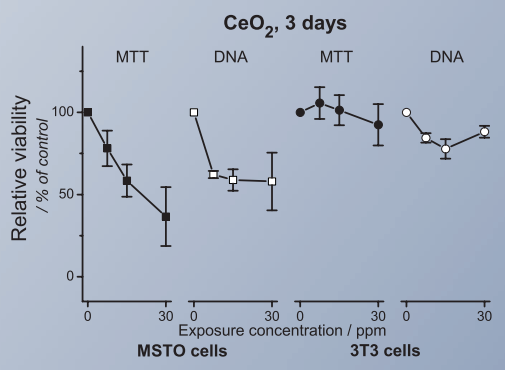
Early risk assessment of nanomaterials may help to avoid costly errors in product development with downstream corrections or market withdrawal. We therefore believe that nanomaterial based products should be developed on a proactive way, e.g. toxiclogical risk assessment should accompagny early proof of concept studies.



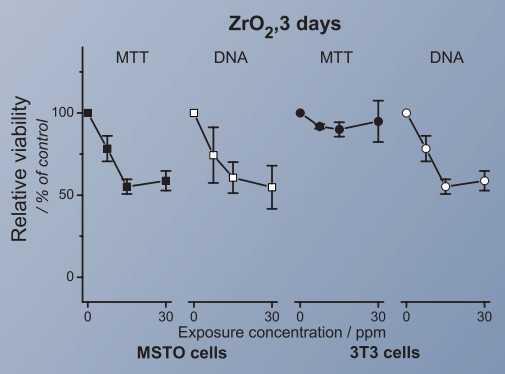


Ceria (CeO_2)
Used i. e. in semiconductor polishing, catalysis
rapidly growing market
ceramic, hard, insoluble
BET: 124 m^2/g, particle size 6-30 nm

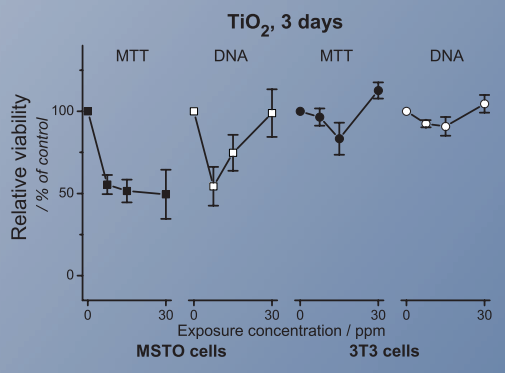




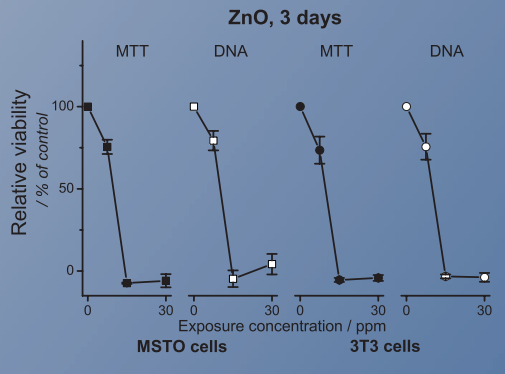
Zirconia (ZrO_2)
Used i. e. used for scratch resistant coatings, medical implants
rapidly growing market
ceramic, hard, insoluble
BET: 96 m^2/g, particle size 10-30 nm



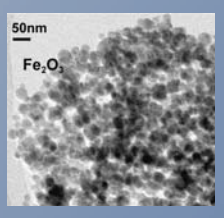
Titania (TiO_2)
Used i. e. as pigment, in sun screens
huge existing pigment market,
large scale application in cosmetics
ceramic, insoluble
BET 188 m^2/g, particle size 10-50 nm

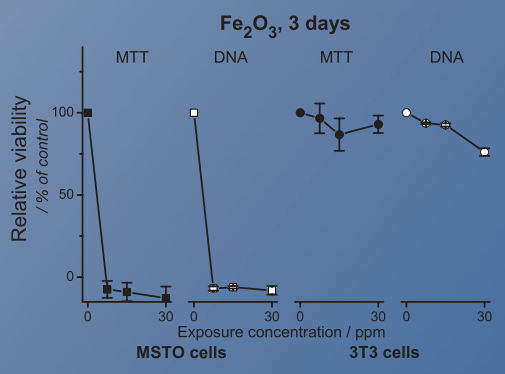


Zinc oxides (ZnO)
Used i. e. in cosmetics, sun screens and polymers
partially soluble
BET: 57 m^2/g, particle size 15-50 nm

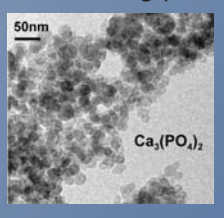


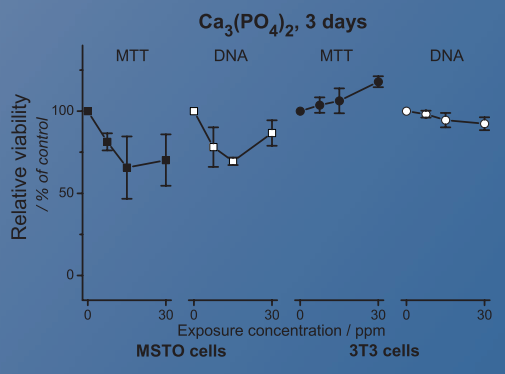
Iron oxides (Fe_2O_3)
Discussed for medical treatments, magnetic drug targeting
magnetic resonance imaging
partially soluble
BET: 93 m^2/g, particle size 10-50 nm





Tricalcium phosphate ($Ca_3(PO_4)_2$)
Used in implant materials
biocompatible
soluble
BET: 92 m^2/g, particle size 10-50 nm





References

T.J. Brunner, P. Wick, P. Manser, P. Spohn, R.N. Grass, L.K. Limbach, A. Bruinink, W.J. Stark, In Vitro Cytotoxicity of Oxide Nanoparticles: Comparison to Asbestos, Silica, and the Effect of Particle Solubility, Env. Sci. Technol., 40, 4374-81(2006).

L.K. Limbach, Y. Li, R.N. Grass, T.J. Brunner, M.A. Hintermann, M. Muller, D. Gunther, W.J. Stark, Oxide Nanoparticle Uptake in Human Lung Fibroblasts: Effect of Particle Size, Agglomeration and Diffusion at Low Concentration, Env. Sci. Technol., 39, 9370-76 (2005).

Project financing: Bundesamt für Gesundheit, BAG Switzerland.