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Copper oxide nanoparticles: Impact on alveolar epithelial-like cells following air-liquid interface exposure

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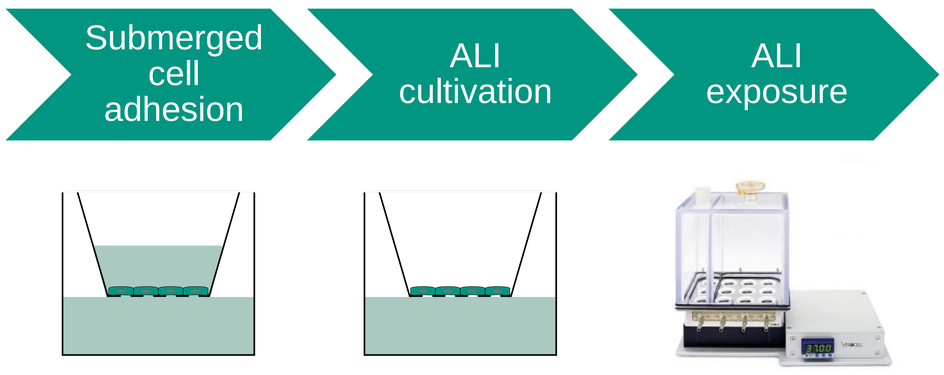
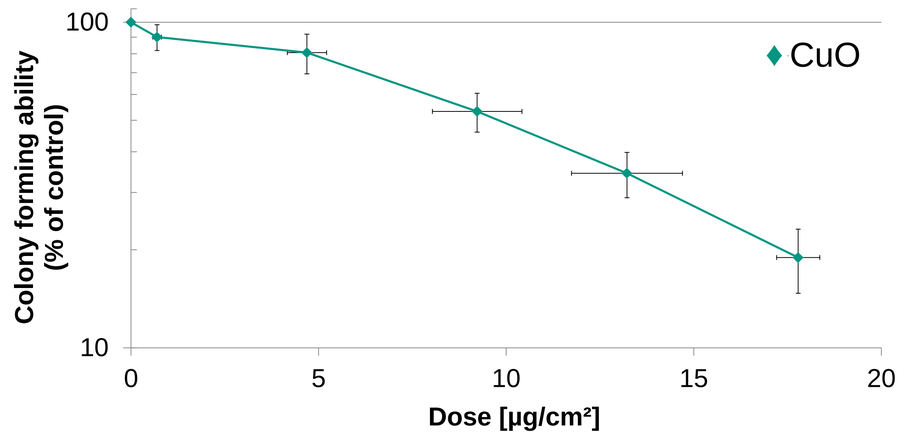
Introduction

The increased use of nanomaterials is the driving force for increasing research on nanotoxicology. In contrast to the traditionally used submerged application, we used an innovative exposure method (air-liquid interface – ALI) which represents a more realistic exposure scenario for investigating airborne nanoparticles (NP). Additionally, the use of ALI exposure systems, e.g. VITROCELL® Cloud, enables the measurement of actual particle depositions, when equipped with a quartz crystal microbalance Within this study, adenocarcinoma human alveolar epithelial-like cells (A549) were exposed to copper oxide (CuO) NP at different doses in the VITROCELL® Cloud. Subsequently, cytotoxic effects were determined using the colony formation assay (CFA). Furthermore, the impact of CuO NP on genomic stability was investigated via high-throughput RT-qPCR gene expression analyses.

ALI exposure - methodology



Cytotoxicity of CuO NP



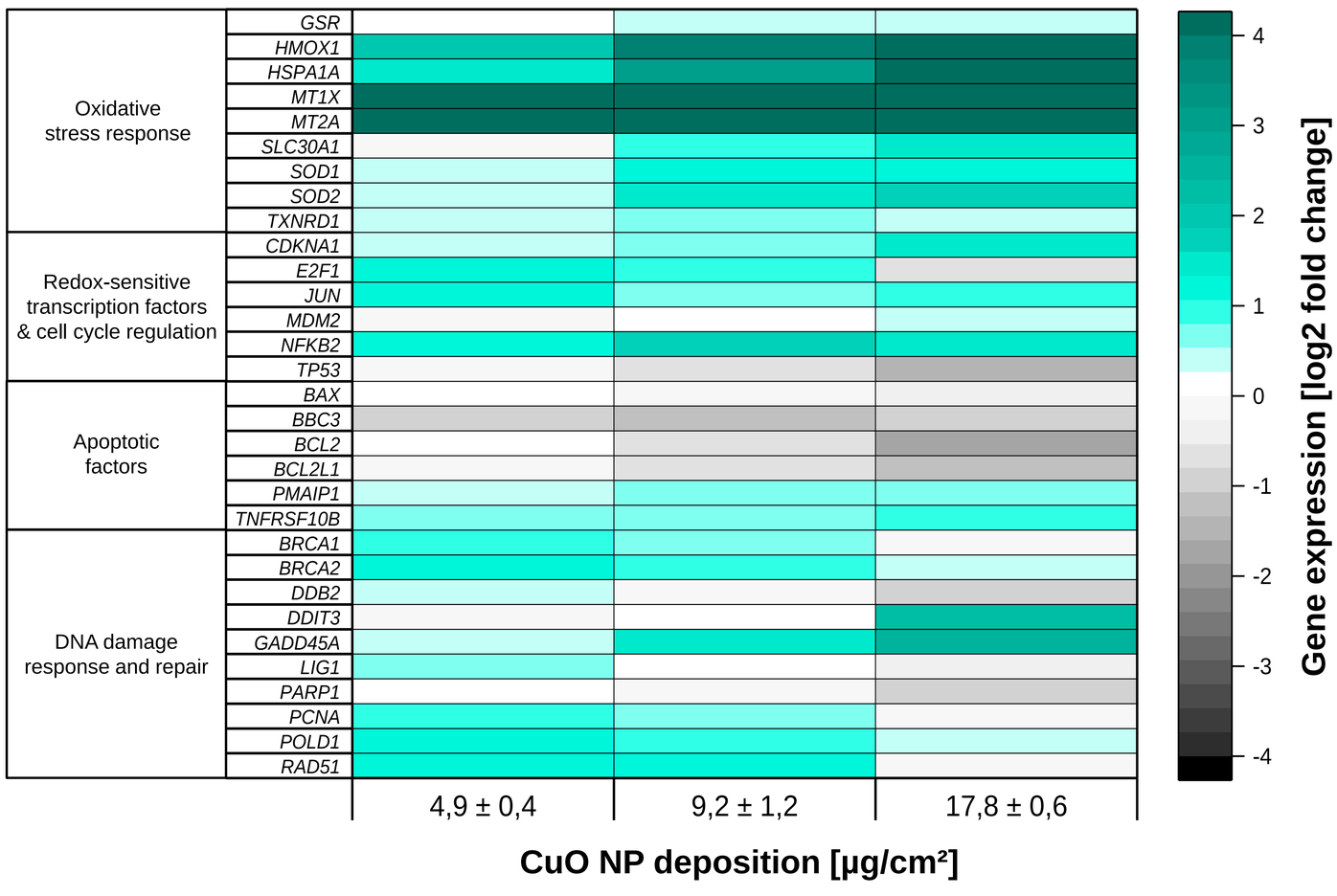
The exposure to CuO NP revealed a dose-related cytotoxicity after 24 h incubation.

CuO NP – impact on gene expression

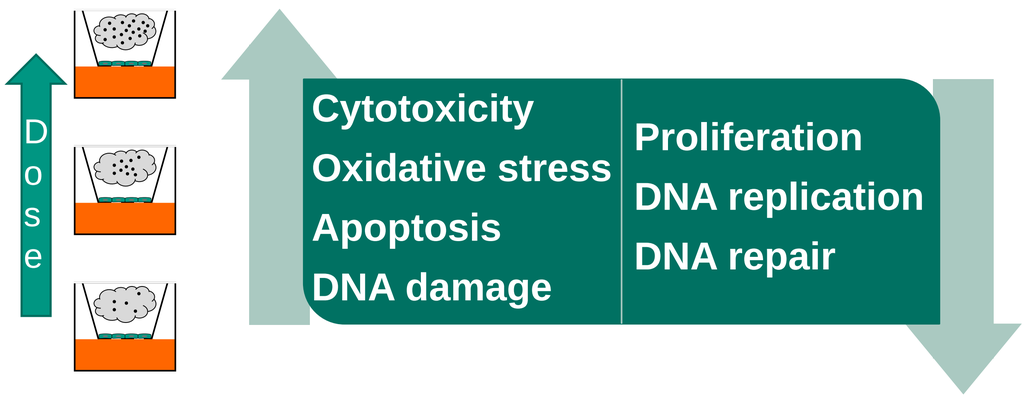
Gene expression profiles were obtained using high-throughput RT-qPCR [1].

The impact of CuO NP on gene expression indicated:

- ❖ *MT1X, MT2A, SLC30A1* ↑
  - → **Intracellular metal overload**
- ❖ *HMOX1, HSPA1A, SOD1, SOD2, GSR, TXNRD1* ↑
  - → **Induction of oxidative stress**
- ❖ *JUN, NFKB2* ↑ low dose: *E2F1* ↑ high dose: *CDKN1A* ↑
  - → Activation of redox-sensitive transcription factors
  - → Enhanced proliferation at low dose
  - → Induced cell cycle arrest with an increasing dose
- ❖ *BAX, BBC3, BCL2, BCL2L1* ↓ *PMAIP1, TNFRSF10B* ↑
  - → **Slight apoptotic effects for mid and high dose**
- ❖ *GADD45A. DDIT3, BRCA2, RAD51, POLD1, PCNA* ↑
  - → **Induction of DNA damage**
  - → **Enhanced DNA replication and DNA double-strand break repair**



Summary



Dose-related events following CuO NP exposure.

Reference

[1] Fischer, B.M., Neumann, D., Piberger, A.L. et al. Arch Toxicol (2015). doi:10.1007/s00204-015-1621-7

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