response and inflammatory reactions via their influence on oxidative stress through the production or scavenging of reactive oxygen species. This study investigates the effect of CeO_2 NPs with different redox activities on inflammasome activation and the maturation of dendritic cells, in three different *in vitro* assays. The biological mechanisms tested in these *in vitro* assays are expected to play a role in the toxic effects observed after inhalation of NPs *in vivo*. NPs with different redox activities were produced by altering the ratio of cerium and zirconium in a ceria zirconia solid solution in the series $Ce_{1-x}Zr_xO_2$ where $x = 0$, 0.25, 0.5, 0.75 and 1. Inflammasomes are intracellular protein complexes that upon sensing danger signals can initiate inflammatory responses. To measure inflammasome activation, THP-1 human monocytes were differentiated to macrophages by PMA. After exposure of THP-1 derived macrophages to CeO_2 NPs for 48 h, cell viability decreased and interleukin-1β production increased, indicating inflammasome activation. CeO_2 NPs with more zirconium induced less toxicity in THP-1 cells, but seemed to have a similar effect on inflammasome activation. Dendritic cells (DCs) play an important role in the innate as well as the adaptive immune response. Human peripheral blood mononuclear cells were cultured for 6 days to obtain immature DCs. The immature DCs were exposed to CeO_2 NPs or the supernatant of Human Bronchial Epithelial (16HBE) cells exposed to the same CeO_2 NPs. After 48 h of exposure, cell viability decreased, but no dose-related increase in interleukin-12p40 production was observed, indicating no effect on DC maturation. CeO_2 NPs with more zirconium seemed to induce less toxicity in 16HBE cells and DCs, but did not seem to affect DC maturation.

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P08-025
Early exposure to titanium dioxide nanoparticles caused a decrease in the cytoplasmic catalase activity, inducing lipid peroxidation in the *Saccharomyces cerevisae*

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The massive production of nanomaterials has created new pollutants whose interaction with living organisms is unclear. Recent studies have revealed that these materials generate reactive oxygen species, causing cell damage, when antioxidant systems fail, fact which justifies its inclusion in toxicological studies. Thus, the aim of this study was to test if early exposure of *Saccharomyces cerevisiae* to 5 μg/mL of titanium dioxide nanoparticles (TiO_2-NP, size < 100 nm), with heat shock, does not disturb its antioxidant response mediated by superoxide dismutase and catalase activity. *S. cerevisiae* UE-ME$_3$, a wild-type strain belonging to Oenology Laboratory of the University of Évora were grown in YEPG medium (3% glycerol) at 28 °C. At middle-exponential phase 2% glucose (YEPGD) and/or 5 μg/mL TiO_2-NP stock solution were added and cells were grown for 200 min at 28 °C or 40 °C (heat-shock, ST). Culture medium lacking glucose or NPs served as control samples. At the end of the experiment, the dry weight was determined and remaining cells were disintegrated in 10 mM phosphate buffer pH 7.0 by ultra-sonication. The post-12,000 × *g* supernatant was used for determination of MDA content and catalase (CTT1) and tase (SOD2). The results showed that the presence of glucose in the medium caused an increase of biomass, a decrease in the MDA content and CTT1 activity without change CTA1, SOD1 and SOD2 activity. Additionally, it was determined an increase in CTA1, SOD1 and SOD2 activity in the cells grown in YEPGD-ST medium. The NP-TiO_2 exposure with ST, decreased CTT1 activity for similar levels to those estimated in the cells grown in YEPGD medium with nanoparticles, did not affect the CTA1 and SOD1 activity, increased the MDA level and kept the SOD2 activity in similar levels to those detected in cells grown in YEPGD-ST medium. The decrease in the CTT1 activity caused by NPs may justify, in part, the increase in MDA level.

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Evaluation of molecular responses following workplace-relevant inhalation exposure to MWCNT

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Pulmonary toxicity from multi-walled carbon nanotube (MWCNT) exposure includes epithelial hyperplasia, inflammation, and fibrosis. However, the contributing molecular mechanisms remain undefined particularly at exposure levels relevant to the workplace. To address this, a dose-response 4-wk inhalation exposure to MWCNT in mice with daily alveolar depositions of 1970 ng, 197 ng, and 19.7 ng was done. Cumulatively, these doses represent 76, 7.6, and 0.76 years for the high, middle, and low dose, respectively, for a worker exposed to a workplace-derived inhalable concentration of 10.6 μg/m^3. Mice were sacrificed at 0, 28, and 84 d post-exposure and pulmonary global gene expression results were analyzed by QIAGEN's Ingenuity Pathway Analysis. These results were compared to bronchoalveolar lavage (BAL) protein levels and histopathology. The number of differentially expressed genes were time- and dose-dependent. The upstream regulator analysis, a more informed interpretation of the connections from differentially expressed genes, showed significant alterations for the high dose with > 135 activated regulators at every time point post-inhalation. The middle dose had < 10 upstream regulators predicted at any time point and the low dose had zero. The inflammatory regulators (e.g. IL-1b, IL-6, NFkB) were activated throughout in the high dose, but only expressed early in the middle dose and not sustained. These findings were reflected in BAL inflammatory protein levels. Regulators associated with pathological changes (TGFb, EGF, PDGF) were also associated with the high dose exposure. The middle dose had increased fibrotic markers at 0 and 28 d by BioProfiler analysis that were absent by 84 d. This was confirmed by morphometric analysis of alveolar fibrillary collagen thickness which revealed a significant increase in the high dose, a non-significant trend in the middle dose, and no change in the low dose exposure group. These results confirm the potential of MWCNT to induce molecular mechanisms associated with inflammation and pathological changes and provide context to relevant workplace exposure levels.

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