Abstract

Human exposure to particulate matter (PM) is a global environmental health concern. Zinc (Zn(2+)) is a ubiquitous respiratory toxicant that has been associated with PM health **effects**. However, the molecular mechanism of Zn(2+) toxicity is not fully understood. H2O2 and Zn(2+) have been shown to mediate signaling leading to adverse cellular responses in the lung and we have previously demonstrated Zn(2+) to cause cellular H2O2 production. To determine the role of Zn(2+)-induced H2O2 production in the human airway epithelial cell response to Zn(2+) exposure. BEAS-2B cells expressing the redox-sensitive fluorogenic sensors HyPer (H2O2) or roGFP2 (EGSH) in the cytosol or mitochondria were exposed to 50μM Zn(2+) for 5min in the presence of 1μM of the zinc ionophore pyrithione. Intracellular H2O2 levels were modulated using catalase expression either targeted to the cytosol or ectopically to the mitochondria. HO-1 mRNA expression was measured as a downstream marker of response to **oxidative** stress induced by Zn(2+) exposure. Both cytosolic catalase overexpression and ectopic catalase expression in mitochondria were effective in ablating Zn(2+)-induced elevations in H2O2. Compartment-directed catalase expression blunted Zn(2+)-induced elevations in cytosolic EGSH and the increased expression of HO-1 mRNA levels. Zn(2+) leads to multiple **oxidative effects** that are exerted through H2O2-dependent and independent mechanisms.