## Synergistic Effect of Co-Exposure to SOA and Transition Metals Induces Toxicity and Developmental Defects in vitro and in vivo

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Particulate matter (PM) is one of the biggest factors endangering human health, which leads to millions of premature deaths. Secondary organic aerosol (SOA) is an aerosol formed by multiple oxidation reactions of volatile organic compounds (VOC) or semi-organic compounds in the atmosphere, which is one of the main components of suspended particles in the air. SOA can cause various adverse health conditions, but little is known about the effects of the interaction between SOA and transition metal ions on the human body. In this study, we conducted in vitro and in vivo experiments. In vitro experiments, we used human lung cancer cell line A549 cells to study the cytotoxicity of different types of SOA (4-NC, 4-NP and 3-NP) and different common transition metal ions (Cu, Mn). In vivo experiments, we used zebrafish embryos as a model system to study the developmental toxicity of water-soluble SOA or transition metal ions under co-exposure. We found that its synergistic toxicity can cause pericardial edema and developmental defects in zebrafish larvae, and behavioral experiments also showed that exposure to 4-NP and transitional metal ions (Mn) caused a significant decrease in the migration distance of zebrafish larvae. In addition, we also found that the synergistic cytotoxicity of 4-NP and manganese (Mn) reduced the expression of antioxidant enzyme SOD and nuclear transcription factor Nrf2 in zebrafish larvae, and the Western dot blot experiment also showed that SOD and Nrf2 were significantly reduced in protein expression.