Genotoxic responses to nanomaterials and metal(loid)s co-exposure: insights from complementary DNA damage biomarkers

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Background: Human exposure to nanomaterials (NMs) and metal(loid)s rarely occurs in isolation, yet toxicological studies still predominantly assess single substances. Co-exposure scenarios may alter both the magnitude and the type of DNA damage induced. The Comet and the γ-H2AX assays represent complementary approaches for detecting DNA damage and DNA double-strand breaks, respectively, providing insight into genotoxic responses.

Aim: This study investigated the genotoxic effects of NMs and metal(oid)s under single and binary co-exposure conditions, evaluating whether the latter alters the extent and nature of DNA damage.

Methods: Two human cell models (A549 and HepG2) representing distinct target tissues were exposed to individual contaminants and binary mixtures. Primary DNA damage and oxidative lesions were assessed using a medium-throughput Comet assay and its FPG-modified version. DNA double-strand breaks were evaluated through quantification of γ-H2AX formation by flow cytometry. Responses following single and combined exposures were compared to identify potential interaction patterns.

Results: Single exposures to metal(loid)s resulted in marked increases in primary DNA damage, while NMs alone induced modest and cell-type-dependent effects (more pronounced in HepG2 cells). Co-exposure responses differed between cell models but frequently resulted in enhanced primary DNA damage relative to NMs exposures alone. In contrast, γ-H2AX analysis revealed that co-exposure generally reduced double-strand break formation compared with the corresponding single metal(loid) exposures, particularly in A549 cells, whereas HepG2 showed intermediate responses. These findings suggest that co-exposure may modify the severity and mechanisms of DNA damage, potentially shifting responses toward less severe lesion types. Some co-exposure conditions also indicated reduced oxidative DNA damage compared with exposure to single compounds.

Conclusions: The use of complementary genotoxicity biomarkers demonstrates that co-exposure can modulate both the extent and the nature of DNA damage. These results highlight the importance of incorporating co-exposure scenarios and multiple mechanistic endpoints in environmental mutagenesis and risk assessment studies.

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