

## **Genotoxic damage, immunotoxicity, gene expression signature, and circulating miRNAs as biomarkers of nanoplastic exposure: A pilot study in human-exposed population**

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Nanoplastics (NPLs) are widespread environmental contaminants that can enter the human body through inhalation, ingestion, or dermal contact. Once internalized, they may cross biological barriers and accumulate in tissues, potentially inducing oxidative stress, inflammation, and genotoxicity. However, the health risks associated with NPL exposure remain unclear due to the lack of specific biomarkers and the analytical challenges related to their small size and chemical diversity.

To address this gap, we aimed to identify and validate novel molecular biomarkers of NPL exposure. *Ex vivo* experiments were conducted using blood from healthy donors to detect changes in gene expression in peripheral blood immune cells and alterations in circulating miRNAs in plasma. These candidate biomarkers were then evaluated in a pilot study involving textile workers occupationally exposed to NPLs and compared to non-exposed individuals. Complementary assessments included the comet assay to measure DNA damage and analysis of inflammatory cytokines in plasma.

Our findings revealed distinct gene expression signatures and altered miRNA profiles in both *ex vivo* exposed samples and in occupationally exposed individuals. In addition, exposed workers exhibited significantly increased DNA damage and higher levels of inflammatory cytokines compared to controls.

These results support the relevance of the identified genes and miRNAs as potential biomarkers of NPL exposure and related biological responses.

This study provides novel molecular evidence of NPL-related effects and proposes new tools for biomonitoring in both environmental and occupational health contexts. The findings underline the urgent need for preventive strategies and regulatory policies aimed at reducing NPL exposure and protecting public health.

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