

Chronic exposure to nanoplastics alters stem cell type-specific mechanisms, promoting cancer development

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Micro- and nanoplastics (MNPLs) are increasingly recognized as a potential threat to human health. These small plastic particles can be internalized in primary organs, translocate through physiological barriers, reach the bloodstream and potentially bioaccumulate in secondary organs. Increasing evidence demonstrates potential long-term impacts of MNPLs, including carcinogenicity. However, the molecular mechanisms leading to these effects are largely unexplored.

In this work, we compared the pre-neoplastic effects of polystyrene (PS) and polyethylene terephthalate (PET) nanoplastics on mammary stem cells, which may be especially sensitive to the cumulative impacts of environmental pollutants due to the long lifespans in the human body. Both plastic types induced similar oncogenic outcomes, particularly when combined with physiologically relevant microenvironmental signalling such as BMP2, a key regulator of stem cell niche. Notably, a comprehensive omic analysis revealed that the molecular mechanisms leading to these effects are different for PS and PET. While PS mainly activates kinase networks, PET induced large transcriptional deregulations. Besides, our approach allowed us to identify a molecular signature especially affected by MNPL exposure and comprised of genes associated with poorer overall survival in patients with breast cancer.

Our work underscores the urgent need to refine current approaches and to incorporate a mechanistic perspective for risk assessment. Further, our findings support the integration of stem-cell based assays, microenvironmental factors and realistic test materials in testing frameworks to inform regulation and support decision-making to mitigate the impact of MNPLs.

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