Long-term exposure to secondary polyethylene terephthalate nanoplastics induces carcinogenesis *in vitro*

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Micro-/nanoplastics (MNPLs) are environmental contaminants originated mainly from plastic waste degradation that pose potential health risks. Inhalation is a major exposure route, as evidenced by their detection in human lungs, with polyethylene terephthalate (PET) among the most abundant particles in respiratory airways. However, the harmful effects of particle bioaccumulation remain unclear, as chronic effects are understudied. To assess long-term effects, specifically carcinogenic effects, BEAS-2B cells were exposed to PET-NPLs for 30 weeks. Genotoxicity, carcinogenic phenotypic hallmarks, and a panel of genes and pathways associated with cell transformation and lung cancer were examined and compared across three exposure durations. No significant effects were observed after 24 hours or 15 weeks of exposure. However, 30-week exposure led to increased genotoxic damage, anchorage-independent growth, and invasive potential. Transcriptomic analysis showed upregulation of several oncogenes and lung cancer-associated genes at the end of the exposure. Further analysis revealed an increase in differentially expressed genes over time and a temporal gradient of lung cancer-related genes. Altogether, the data suggest PET-NPLs' potential carcinogenicity after extended exposure, highlighting serious long-term health risks of MNPLs. Assessing their carcinogenic risk under long-term chronic, real-life conditions is crucial to address knowledge gaps and eventually develop preventive policies.

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