Exploring the Carcinogenic Potential of PET Nanoplastics Co-exposure with Cigarette Smoke Condensate: A Long-Term In Vitro Study Using BEAS-2B Cells

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Air pollution stands as a primary contributor to global disease and premature mortality, responsible for over 7 million premature deaths annually. Among its contemporary concerns, micro and nanoplastics (MNPLs) have garnered significant attention due to their detection within human lungs, with polypropylene (PP) and polyethylene terephthalate (PET) fibers emerging as predominant species. Despite existing studies examining the impacts of certain MNPLs in animal and *in-vitro* models, they typically focus on short-term exposures, failing to capture the reality of persistent, cumulative exposure and bioaccumulation. Addressing this critical gap, our research simulates real-life scenarios through a novel long-term exposure study utilizing BEAS-2B human bronchial epithelial cells. In a previous assessment, BEAS-2B cells were continuously exposed to true-to-life polyethylene terephthalate nanoparticles (NPET), with evaluations conducted at various intervals to assess cell transformation biomarkers. At the conclusion of a 30-week exposure period, NPET-exposed cells exhibited elevated genotoxic DNA damage and an increased anchorage-independent growth ability compared to control cells. These findings, coupled with observations of PET-induced tumor promotion in the OECD's Bhas-42 cell transformation assay (CTA), denote the induction of a "prone to transformation progress (PTP)" phenotype in the BEAS-2B cell line under prolonged NPET exposure. To accelerate this transformation process, PTP cells were subjected to 4-week co-exposure to NPET and cigarette smoke condensate (CSC), followed by a reassessment of biomarkers. The NPET-CSC co-exposed cells exhibited significantly greater total DNA damage compared to non-exposed cells and those solely exposed to CSC. While colony size remained consistent across treatments, the number of colonies and their migratory and invasive capabilities were notably enhanced in PET and NPET-CSC exposed cells. Utilizing cell transformation biomarkers, our study demonstrates the oncogenic potential of long-term NPET exposure in BEAS-2B cells, emphasizing the relevance of investigating MNPL effects under conditions mirroring contemporary human exposures.

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