Long-term exposure to PS and PET nanoparticles in human lung cells

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Plastic properties, such as chemical stability, easy handling, high malleability, or good resistance, have promoted the massive use of these materials in a vast variety of applications. The exponential production of these polymers, along with an inefficient recycling system, has resulted in an alarming environmental accumulation of plastic waste. The degradability of these polymers in the environment results in the so-called micro and nanoplastics (MNPLs). These ubiquitous tiny particles have been identified in all the ecosystems, ranging from abiotic environments to higher organisms. In humans, besides ingestion which has already been pointed out as an important route of exposure to MNPLs, attention is now paid to inhalation, considered also as a major source of exposure. Although MNPLs have recently been identified in the lungs of living people, very little is known about their chronic effects on human health. The purpose of this study is to identify the long-term adverse effects of two of the most common inhalable MNPLs: polystyrene (PS) and polyethylene terephthalate (PET). For that, Beas-2B (bronchial cell line) and A549 (alveolar cell line) have been exposed up to 15 weeks and different effects were evaluated. By using a battery of i*n vitro* assays, we have determined the ability of MNPLs to reach cell cytoplasm, their genotoxic potential, and some cell transformation hallmarks, like proliferation rate, anchorage-independent growth, migration potential, invasion ability, and tumorsphere generation.

Our results show a high ability of PS and PET NPLs to be uptake by the cell, although no genotoxic nor carcinogenic potential has been anticipated until now. We wish to point out the relevance of the *in vitro* approach used for assessing the carcinogenic potential of the MNPL. We propose our battery of hallmarks as an appropriate way to assess the carcinogenic potential of MNPLs, as it has been previously demonstrated for other agents, including several nanoparticles.

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