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In Vitro Intestine Tissue Model to Study the Impact of Plastic Particles

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Abstract : Micro- and nanoplastics' (MNLPs) omnipresence and ecological accumulation is evident when surveying recent environmental impact studies. For example, in 2014 it was estimated that at least 52.3 trillion plastic microparticles are floating at sea, and scientists have even found plastics present remote Arctic ice and snow (5,6). Plastics have even found their way into precipitation, with more than 1000 tons of microplastic rain precipitating onto the Western United States in 2020. Even more recent studies evaluating the chemical safety of reusable plastic bottles found that hundreds of chemicals leached into the control liquid in the bottle (ddH2O, ph = 7) during a 24-hour time period. A consequence of the increased abundance in plastic waste in the air, land, and water every year is the bioaccumulation of MNLPs in ecosystems and trophic niches of the animal food chain, which could potentially cause increased direct and indirect exposure of humans to MNLPs via inhalation, ingestion, and dermal contact. Though the detrimental, toxic effects of MNLPs have been established in marine biota, much less is known about the potentially hazardous health effects of chronic MNLP ingestion in humans. Recent data indicate that long-term exposure to MNLPs could cause possible inflammatory and dysbiotic effects. However, toxicity seems to be largely dose-, as well as size-dependent. In addition, the transcytotic uptake of MNLPs through the intestinal epithelia in humans remain relatively unknown. To this point, the goal of the current study was to investigate the mechanisms of micro- and nanoplastic uptake and transcytosis of Polystyrene (PE) in human stem-cell derived, physiologically relevant in vitro intestinal model systems, and to compare the relative effect of particle size (30 nm, 100 nm, 500 nm and 1 µm), and concentration (0 µg/mL, 250 µg/mL, 500 µg/mL, 1000 µg/mL) on polystyrene MNLP uptake, transcytosis and intestinal epithelial model integrity. Observational and quantitative data obtained from confocal microscopy, immunostaining, transepithelial electrical resistance (TEER) measurements, cryosectioning, and ELISA cytokine assays of the proinflammatory cytokines Interleukin-6 and Interleukin-8 were used to evaluate the localization and transcytosis of polystyrene MNPs and its impact on epithelial integrity in human-derived intestinal in vitro model systems. The effect of Microfold (M) cell induction on polystyrene micro- and nanoparticle (MNP) uptake, transcytosis, and potential inflammation was also assessed and compared to samples grown under standard conditions. Microfold (M) cells, link the human intestinal system to the immune system and are the primary cells in the epithelium responsible for sampling and transporting foreign matter of interest from the lumen of the gut to underlying immune cells. Given the uptake capabilities of Microfold cells to interact both specifically and nonspecific to abiotic and biotic materials, it was expected that M- cell induced in vitro samples would have increased binding, localization, and potentially transcytosis of Polystyrene MNLPs across the epithelial barrier. Experimental results of this study would not only help in the evaluation of the plastic toxicity, but would allow for more detailed modeling of gut inflammation and the intestinal immune system.

Keywords : nanoplastics, enteroids, intestinal barrier, tissue engineering, microfold (M) cells
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