Effects of the *in vitro* digestive process on the toxicological profile of polystyrene nanoplastics in different human hematopoietic cell lines

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In the past few years, growing production/consumption of plastic have turned plastics into the world's largest polluter. Plastics released into the environment reduce their size range into micro-nano plastics (MNPLs) by the effects of many environmental agents. Human exposure to MNPLs can be through ingestion, airborne inhalation, or dermal exposure. However, oral ingestion is considered the major exposure route. Once MNPLs enter the human body via the oral route they must pass through different compartments of the gastrointestinal tract that may affect physicochemical properties and surface features. Probably one of the most important parameters that digestion could affect is the formation of the protein corona, affecting biological interactions and intestinal uptake of particles. To effectively analyze the toxicity of MNPLs, the influence of the digestive tract environment should be considered. Polystyrene micro-nano plastics (PS-MNPLs) are one of the most frequently observed MNPLs in the environment. PS-MNPLs have demonstrated their ability to translocate from the intestinal mucosal tissues and access the blood and lymphatic circulation. For this reason, the aim of this study is to determine the influence of the digestive process on the toxicity of PS-NPLs in three different human leukocytic cell lines: Raji-B (B-lymphocytes), TK6 (lymphoblasts) and THP-1 (monocytes).

An *in vitro* digestion assay was performed on pristine PS-NPLs (50 nm). Using transmission electron microscopy (TEM-EDX), scanning electron microscopy (SEM- TDX), and Z-sizer, PS-NPLs were characterized. The three cell lines were exposed to different concentrations of *in vitro* digested PS-NPLs (dPS-NPLs). Cytotoxicity, reactive oxygen species (ROS) production, and genotoxicity were assessed at different time points. Preliminary results show no significant cytotoxicity effects in the cell lines. Only moderate effects were observed at the highest concentration of dPSNPs in TK6 at 48 h exposure. Regarding intracellular ROS production measured by flow cytometry with DHE, a slight increase of ROS production was observed in TK6 and Raji-B cell lines at 24 h of exposure, but without reaching statistically significant. Additionally, the comet assay is going to be assessed to measure the levels of genotoxic and oxidative DNA damage.