Polylactic acid nanoplastics (PLA-NPLs) induce adverse effects on an *in vitro* model of the human lung epithelium: the Calu-3 air-liquid interface (ALI) barrier

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The expected increments in the production/use of bioplastics, as an alternative to petroleum-based plastics, require a deep understanding of their potential environmental and health hazards, mainly as nanoplastics (NPLs). Since one important exposure route of NPLs is inhalation, here we aimed at studying the fate and effects of true-to-life polylactic acid nanoplastics (PLA-NPLs), using the *in vitro* Calu-3 model of bronchial epithelium under air-liquid interphase exposure conditions. To determine the health risk of PLA-NPLs in a more realistic scenario, both acute (24 h) and long-term (1 and 2 weeks) exposures were performed. Results indicate that PLA-NPLs internalized easily in the barrier (~10% at 24 h and ~40% after 2 weeks), affecting the expression of tight-junctions formation (~50% less *vs* control) and the mucus secretion (~50% more *vs* control). Interestingly, significant genotoxic effects (DNA breaks) were detected by using the comet assay, long-term effects being more marked than acute (7.01 *vs* 4.54% of DNA damage). When an array of cellular proteins including cytokines, chemokines, and growth factors were used, a significant over-expression was mainly found in long-term exposures (~20 proteins *vs* 5 proteins after the acute exposure). Overall, these results describe the potential hazards posed by PLA-NPLs, under relevant long-term exposure scenarios, highlighting the advantages of the model used to study bronchial epithelium tissue damage and signaling endpoints related to inflammation.