Stemness imbalance and oncogenic effects induced by *in vitro* chronic exposure to PS and PET nanoplastics in breast progenitor cells

I. Barguilla[1], B. Guyot[1] and V. Maguer-Satta[1]

[1] *Centre de Recherche en Cancérologie de Lyon, Inserm U1052-CNRS UMR5286, Centre Léon Bérard, Lyon, France.*
E-mail: irene.barguilla-moreno@lyon.unicancer.fr

The widespread presence of micro- and nanoplastics (MNPLs) in the environment is rising concerns regarding their potentially harmful effects on human health. They easily enter the human body and have the ability to translocate through physiological barriers. Indeed, MNPLs have already been detected in blood and lung tissue. The number of studies focused on their effects on health is progressively increasing, generally linking MNPLs exposure with mild but relevant effects in terms of cytotoxicity, ROS generation, DNA damage, and pro-inflammatory response alterations. These endpoints have been mainly explored at the short term; however, plastic particles are well-known for their persistence in the environment and this feature is expected to also occur in tissues. MNPLs' bioaccumulation extended in time could lead to molecular adverse effects such as mutagenesis and carcinogenesis, an aspect insufficiently explored until now.

Stem cells are among the most persistent cell types, with lifespans ranging from months to several years. This makes them likely targets of persistent pollutants as is the case of MNPLs. Therefore, this study aims to evaluate the long-term effects of polystyrene- (PS-NPLs) and polyethylene terephthalate (PET-NPLs) nanoplastics on MCF10A, a model of breast progenitor cells with known potential to go through malignant transformation. We have developed an *in vitro* approach in which we continuously exposed the cells for 12 weeks to PS- or PET-NPLs in combination with BMP_2 and IL-6, which mimic an inflammatory microenvironment. At several time points during the chronic exposure, we have monitored the cell's differentiation and transformation status. The colony-forming-cell (CFC) assay and the mammosphere formation assay have shown a differential effect of PS- and PET-NPLs on MCF10A differentiation, while no significant indications of cell transformation have yet been observed with the soft agar assay. Ongoing work is focused on the in-depth characterization of the exposed cells, analyzing several differentiation markers which will contribute with relevant data regarding the impact of MNPLs in cell fate deregulation.