P45

Stem cells as unique models to study long-term effects triggered by micro- and nanoplastic exposure: a focus on cell transformation and differentiation.

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

[1] Cancer Research Center of Lyon, Inserm U1052-CNRS UMR5286, Centre Léon Bérard, Lyon, France.
** irene.barguilla-moreno@lyon.unicancer.fr*

The wide diversity of human exposures across individuals and throughout their lifetime calls for new approaches and models to implement risk assessment strategies. In this context, stem cells offer a unique possibility to study specific functionalities of immature cells, cell fate, and cell transformation. Due to their long lifespans, stem cells can be particularly susceptible to long-term exposures and the accumulation of abnormalities could lead to a differential impact compared to short-lived cells, including the emergence of cancer stem cells. Therefore, we propose stem cells as a relevant model for the evaluation of the potential impact of micro- and nanoplastic (MNPLs) on human health. The population is continuously exposed to these small plastic particles that can translocate through physiological barriers and cause mild but relevant effects related to cytotoxicity, ROS generation, DNA damage, and pro-inflammatory response alterations. The information regarding the bioaccumulation of MNPLs is still limited but the extended exposure could be expected to induce accumulative adverse effects such as mutagenesis and carcinogenesis, aspects insufficiently explored until now.

Our work aims to develop stem cell-based models useful to provide information on the potential long-term effects of MNPLs by evaluating endpoints related to transformation onset and stemness imbalance. On the one hand, we have developed an in vitro exposure approach in which we continuously exposed a model of breast stem cells (MCF10A) to polystyrene (PS) and polyethylene terephthalate (PET) nanoplastics for 5 months. Although we have not identified significant changes in the transformed status of the cells at a functional level, we have observed an increasing tendency in their anchorage-independent growth and migration capacities that points to MNPLs as inducers of a permissive context for cell transformation. Ongoing work is focused on identifying potential underlying molecular effects by transcriptomic and kinase activity profiling analyses. In parallel, we are looking for new stem cell models relevant to evaluate the potential cell fate-deregulating effect of MNPLs exposure that may require further in-depth studies.

This work could contribute with relevant data regarding the impact of MNPLs on cell fate deregulation and stem cell transformation, and further highlight the interest in incorporating stem cell models in risk assessment strategies.

Keywords:
Stem cells; micro- and nanoplastics; long-term exposure; in vitro transformation; stemness imbalance.