Single-cell transcriptomics analysis of *ex vivo* nanoplastic exposed human whole blood as a model to understand their impact on human health

R. Egea[1*], J. Arribas[1], C. Pommerenke[2], R. Marcos[1], & A. Hernández[1]

[1] Group of Mutagenesis, Departament de Genètica i Microbiologia, Universitat Autònoma de Barcelona, 08193 Cerdanyola del Vallès, Spain
[2] Leibniz Institute DSMZ-German Collection of Microorganisms and Cell Cultures, Braunschweig, Germany
** raquel.egea@uab.cat*

Micro/nanoplastics (MNPLs) have emerged as an environmental concern due to their extensive use and ubiquitous presence. Living organisms, including humans, are exposed to them through different routes, being ingestion and inhalation the major ones. Since MNPLs can cross both the intestinal and pulmonary barriers, their presence in the blood compartment is expected. This potential for systemic distribution raises significant concerns about their impact on human health. Consequently, understanding the interactions between MNPLs and human blood is of great value. In this study, human whole blood was exposed *ex vivo* to better mimic real conditions using five different MNPLs: three polystyrene NPLs of around 50 nm (aminated, carboxylated, and pristine forms), together with two real-life MNPLs from polyethylene terephthalate (PET) and polylactic acid (PLA) of around 150 nm. Single cell RNA sequencing (scRNA-seq) was performed and analysed over different blood cell types and treatments. A high number of differentially expressed genes (DEGs) were identified and values from different blood cell types and treatments were compared. A functional analysis of DEGs was performed and enriched pathways and terms were identified. Results were compared to previous biological assays results finding concordances among them. Results showed a broad response involving different molecular mechanisms. For the first time, the response to a variety of nanoplastic particles has been analysed at the single cell transcriptomics level in humans.

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