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► **To cite this version:**

Véronique Collin-Faure, Bastien Dalzon, Anaelle Torres, Thierry Rabilloud. PARTICLE SHAPE AND INTRINSIC CELLULAR VARIABILITY SHAPE THE RESPONSES OF MACROPHAGES TO POLYSTYRENE NANO AND MICRO PARTICLES. 8th International Conference on Environmental, Health and Safety issues related to Nanomaterials, nanoSAFE'23 and NanoSafety Cluster joint conference, Jun 2023, Grenoble - Maison Minatec, France. hal-04092916

HAL Id: hal-04092916

<https://hal.science/hal-04092916>

Submitted on 11 May 2023

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TOPIC N° 8

**PARTICLE SHAPE AND INTRINSIC CELLULAR VARIABILITY SHAPE THE RESPONSES OF
MACROPHAGES TO POLYSTYRENE NANO AND MICRO PARTICLES**

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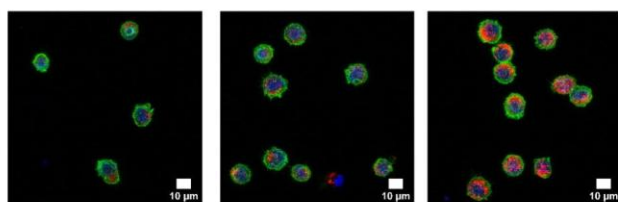
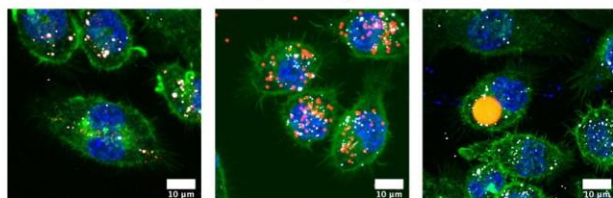
Nanoparticles and among them nanoplastics are generally considered to induce more biological effects than bigger particles because of their greater penetration in bodies and cells. Nevertheless, it is known that particles up to a few microns can translocate through the epithelial barriers and be transported to distal organs. As the particles surface and mass increase with the square and the cube of the size, it may be anticipated that microparticles may induce stronger effects than smaller ones, especially when their size begins to approach the size of the cells.

To investigate this hypothesis, we exposed macrophages (i.e. cells that are able to scavenge particles over a wide size range) to polystyrene particles of 0.1, 1 and 10 µm in diameter, and analyzed their responses by a proteomic approach. This analysis showed an important common core response for the three particles sizes, but also that larger particles induced a more important response than smaller ones at equal mass concentration.

As this suggested a role of the internalized plastic mass in the response, we also investigated an often-overlooked parameter, i.e. the heterogeneity of the cells in their propensity to internalize (plastic) particles. We showed that macrophages vary greatly in their ability to internalize plastic particles. Quite interestingly, “the appetite came with the eating”, so that the final population of cells exposed to a single concentration of plastic particles is indeed a mix of cells with very different loads of internalized plastics. Unsurprisingly, heavily-loaded cells show stronger responses than lightly-loaded cells. We also showed that plastic particles persist in macrophages.

When brought together, these data draw a picture where the maintenance of the function of the immune system is assured by the lightly-loaded cells, while the heavily-loaded cells may induce local effects. This balance may change over time in case of continuous exposure, because of particle accumulation.

Cells having internalized PS beads of various sizes (orange red)
+ test beads (white)



Population heterogeneity after contact with a single
concentration of PS beads