Uptake of polymer-based nanoparticles of different size into multiple cell lines: approaches to control and understand bio-nano interactions

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Abstract

Nanoparticles potentially provide a powerful tool for specific treatments of diseases, acting as a drug delivery transport. However, a deep understanding and control of how nanoparticles interact with biological systems is a key driver to assure the safe implementation of nanomedicine. The overall idea of this project was to provide new leads in the development of such a new field, finding tools for various biomedical applications, not only in drug delivery and gene therapy, but also in molecular imaging and biomarkers, with a better engineered nanoparticle as the ultimate goal. For this we investigated how the basic unit of life, the cell, interacts with nanoparticles. Multiple cell lines were used and the ultimate goal was to control and quantify uptake of a series of negatively charged carboxylated modified polystyrene of different size, understand the endocytic pathways required for NPs internalization, and their final sub-cellular destination. We found that kinetic models can be used to determine uptake and distinguish between uptake of molecules and nanoparticles, based on the competing kinetics of internalization and export from cells. Uptake of nanoparticles is an energy dependent process and it is linear in the first hours, saturating only at longer time scales, due to cell division[1]. Moreover, was found that internalization of nanoparticles is highly size dependent for all cell lines studied, with the different cell types showing very different uptake efficiencies for same materials, with macrophages having the higher uptake rate for all nanoparticle sizes[2] (Figure 1). In the studies of the effects of transport inhibitors, it became very clear that nanoparticle internalization might involve several different mechanisms even in one cell line, although whether this was a result of the lack of inhibitor specificity or evidence of the use of several uptake pathways simultaneously is not yet resolved[3].

References

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Figures

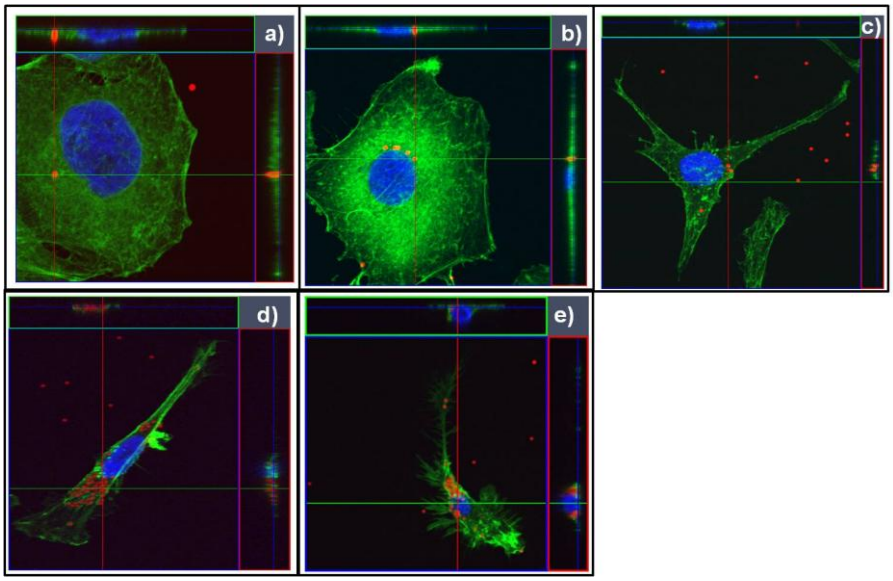

Figure 1- Confocal images of **a)** HeLa, **b)** A549, **c)** 1321N1, **d**) HCMEC/D3, **e)** RAW 264.7 cells treated for 24h with 20 µg/ml of 1µm diameter carboxylated modified polystyrene particles. Images represent optical section (x, y-axis), with respective projection of the x,z- and y, z-axes of a single cell, after 24h incubation with 20 µg/ml, 1µm diameter carboxylate-modified polystyrene particles.