Synthetic cytonauts: Controlling endocytosis with shape, topology and size

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Abstract

In 1984 Christian deDuve, in "A guided tour of the living cell", coined the term "cytonaut" (cell-navigator), a nanoscopic guide able to enter a living cell and describe its complexity. Although, the deDuveian fictitious explorer is rather impracticable, his idea of using a functional probe to gather information on the cell function is very much topical and yet unmet need in cell biology. Thanks to advances in Nanotechnology we can take inspiration from natural cytonauts (such as viruses) to create synthetic versions that can be implemented to enter cells and navigate its interior to deliver therapeutic cargos or diagnostic tools. While we understand the interactions of particular species with human cells on the molecular level, we still miss the basic understanding of the purpose of physical properties of these natural nano- or micro- particles. Here I will discuss how the shape and size of model nanoparticles affect the interactions with human cells at the level of plasma membrane in endocytic processes and internal trafficking through the endosomal pathways. I will show that the overall efficiency of nanoparticle uptake depends on their shape and size, and various stages of interactions - plasma membrane binding kinetics, membrane dwelling time and rates of internalisation are affected distinctly depending on different physical properties of the particles. I will demonstrate that despite of the same chemistry and molecular interactions, the shape and size of nanoparticles determine the involvement of endocytic proteins, like clathrin light chain in their endocytic processes. The internalised particles exhibited differences in the trafficking pathways. Finally I will correlate membrane level interaction differences with intracellular signalling such as anti-viral response and extrinsic apoptosis and show that these can be engineered by choosing the correct nanomaterial.