Spatiotemporal tracking of intracellular nanoparticles that has multivalent peptide-decoration

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Cells can be recognized by the receptors expressed on their surface, and specific targeting of the cells and tissues is a key challenge in broad range of biomedical research. For better targeted drug delivery and therapeutic treatment, strong binding to cells with a desired receptor profiles while barely binding to other cells is essential. Moreover, intracellular distribution of nanoparticles and their interactions with cellular organelles during the course of intracellular trafficking give a key information in the field of nanomedicine. We formulate optimal design rules for multivalent peptide decorated nanoparticles that allow them to efficiently distinguish target cells based on their receptor profiles, and further investigate the intracellular fates of biodegradable nanoparticles at a single nanoparticle level using a complementary imaging analysis process which combines transmission electron microscopy and super-resolution confocal laser scanning microscopy with fluorescence correlation spectroscopy. The results show that properly designed multivalent targeting of receptor leads specificity toward a chosen receptor, thus demonstrating a general route toward targeting cells without particularly dominant markers. The endocytic pathway internalizes nanoparticles from the plasma membrane to a set of endosomes over time, until they are degraded by the cellular autolysosomes in the perinuclear region. Spatiotemporal tracing of the intracellular behavior of an individual nanoparticle reveals that the nanoparticle is spontaneously released from the endosome and transiently stimulates autophagy. The size of autophagosomes increases over time, while cell viability is maintained. Super-resolution fluorescence imaging further clearly confirms the dynamic nature of autophagosome-trapped nanoparticles. Systematic investigation into the intracellular trafficking of nanoparticles using the complementary imaging tools demonstrated non-cytotoxic biological degradation of the silicon nanoparticles, resulting from chemical inertness and stimulated autophagic clearance. Furthermore, the intrinsic photoluminescence of the silicon nanoparticle is employed to monitor the status of drug payload elution, associated with biodegradation during the course of cellular trafficking. We suggest that combinatorial imaging study will provide insights into strategies for the design of nanoparticles for cellular delivery and low cytotoxicity, as well as the degradative mechanisms behind the intracellular fate of nanoparticles.