Supramolecular Aggregation and Fusion of Lysosomes for Improving Cellular Defense Against Bacteria

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Lysosomes function as the organelles for digesting exogenous and endogenous species acquired during endocytosis, phagocytosis, and autophagy. Lysosomes play an important role in killing microbes and the processing of antigen. During phagocytosis, bacteria are trapped in a phagosome and subsequently it fuses with lysosomes to kill the bacteria effectively. The implication of supramolecular assembly in the pharmaceutical field emerged as a new solution to induce the aggregation and fusion of organelles. To this end, a supramolecular system that induces aggregation of lysosomes was designed to facilitate digestion of bacteria. In this system, MOR-PEG-ADA was synthesized from Morpholine (MOR), Polyethylene glycol (PEG) and 1-Adamantanecarboxylic acid (ADA), to target the lysosome of cells. HA-CB[7] (cucurbit[7]uril (CB[7]) grafted hyaluronic acid (HA))- as a biocompatible molecule, can provide a polymeric network to pull ADA labelled lysosomes to initiate aggregation and fusion of lysosome. Upon internalization, HA polymer may pull lysosomes via the host-guest effect between CB[7] of HA-CB[7] and ADA anchored on the surface of the lysosomes. Under confocal microscopy, little aggregation of lysosomes was observed in the control group. In contrast, the cells treated with MOR-PEG-ADA and HA-CB[7] sequentially were found to elicit aggregation between lysosomes. In the antibacterial assay, the aggregation of lysosomes was demonstrated to diminish the viability of E. coli. In conclusion, MOR-PEG-ADA/HA-CB[7] may offer a new supramolecular approach for improving cellular defense against bacteria with the aggregation of lysosomes.