Stimuli-responsive DNA particles underpin three-agent signaling networks with live bacteria and synthetic cells

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Lipid bilayers play an important role in cellular biology as they act as an active filter between the inner and outer environment of the cell. Their integrity, often associated with proper functioning and vitality of the cells, can be compromised by a number of biological and synthetic agents, including antimicrobial peptides, amyloid aggregates, polymer particles and metal particles with charged coatings. Such agents, frequently considered to be toxic and highly undesirable, have a variety of beneficial applications underpinned by the ability to control membrane leakage, which can be harnessed for biosensing and therapeutics. Here, we present a novel type of synthetic, DNA-based particles capable of disrupting and permeabilising lipid membranes in a controlled manner.[1] The particles have a core-shell structure and self-assemble from cholesterol-modified DNA nanostructures,[2,3,4] forming the membrane-adhesive core, and all-DNA nanoconstructs forming a protective hydrophilic "corona". If unperturbed, the particles are colloidally stable, and their size can be prescribed by changing the annealing protocol leading to self-assembly. The protective corona can be selectively displaced upon exposure to external stimuli (macromolecules, pH changes, light), exposing the hydrophobic core and inducing particle aggregation. If, at this stage, membranes are present, the sticky material will adhere to their surface destabilizing and permeabilising them. Furthermore, the sticky "DNA net" formed upon particle activation is capable of capturing and immobilizing swimming cells as we tested with *E. coli*. This is reminiscent of the action of innate-immune cells, which can eject their genetic material to create an Extracellular Trap to combat pathogens. The ability to both permeabilize liposomes and to trap bacteria, as well as the pH responsiveness of particles can be utilized to create a synthetic three-agent signaling network, in which natural pH gradients from *E. coli* trigger the displacement of protective corona from particles, resulting in a simultaneous bacteria immobilization within a DNA net and cargo release from liposomes. Once released, the cargo molecules can interact with bacteria and force them to respond in a programmed manner.[5]

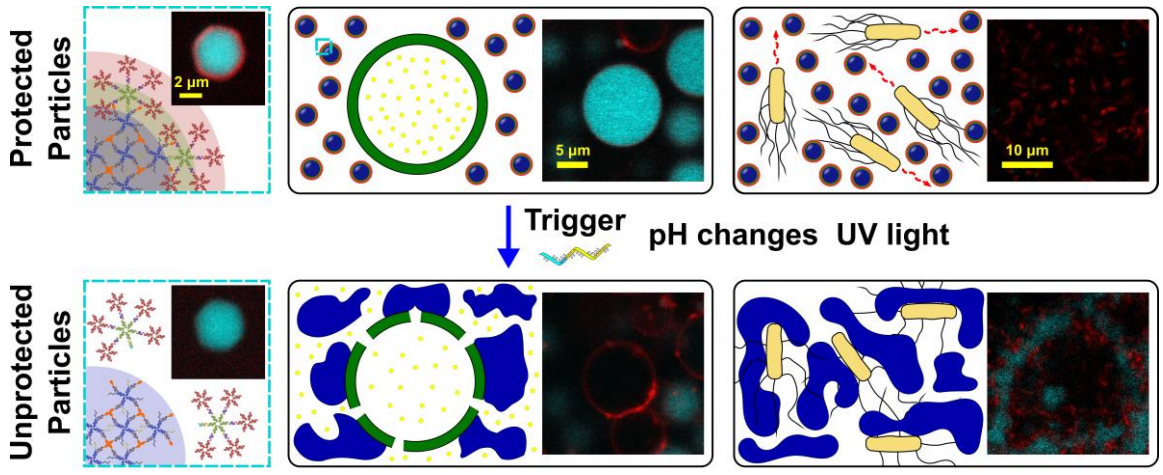

Fig. 1. Particle-induced membrane permeabilization and bacteria entrapment. As a result of exposure to external stimuli (macromolecules, pH changes, light) and subsequent displacement of the hydrophilic corona (left), cholesterol rich particle cores adhere to each other and start to aggregate on the surface of GUVs (middle). DNA aggregation leads to GUV rupture and/or cargo release. Furthermore, once activated, particles form a sticky DNA net, which in turn is able to trap and arrest *E. coli* (right).

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