DNA-Functionalized Nanoparticles for Enhanced Cell-Nanoparticle Interactions

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Nanoparticle attachment to the cell surface is a promising approach to advance the fields of drug delivery, cell functionalization, biosensing, and cell isolation. However, conventional nanoparticle immobilization methods are hindered by poor binding efficiency and reduced cell viability. To address these limitations, we developed a novel strategy for the attachment of nanoparticles to the cell membrane inspired by ligand-receptor molecular recognition. In this work, nanoparticles functionalized with polyvalent DNA nanostructures hybridize with synthetic DNA receptors displayed on cells. In comparison to traditional nanoparticle attachment, this strategy demonstrated an increased binding efficiency and a reduction in cytotoxicity.

Polyvalent DNA-functionalized nanoparticles were synthesized using the hybridization chain reaction and characterized using zeta potential, UV-Vis spectrophotometry, and fluorescence analysis techniques. A clear negative shift in the zeta potential of the nanoparticles was observed immediately after DNA incubation, indicating the stable modification of nanoparticle with DNA. Further, the polyvalent DNA nanoparticles showed an increase in peak absorbance and fluorescence of at least 5-fold in comparison to a monovalent DNA nanoparticle, supporting the presence of a repeating DNA nanostructure.

Cell membrane attachment was examined via flow cytometry and confocal laser scanning microscopy (CLSM). Fluorescence quantum dots were utilized to clearly demonstrate immobilization on the cell surface. Under identical incubation parameters, the mean fluorescent intensity of polyvalent DNA nanoparticles is shown to be nearly one order of magnitude greater than the conventional attachment methods. This data suggests that this DNA-based ligand-receptor strategy can achieve a nearly 10-fold increase in nanoparticles bound to the surface of the cell. Thus, polyvalent DNA-functionalized nanoparticles boast great potential to progress various biomedical applications, including nanoparticle delivery, cell delivery, and biosensing.