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Energy Transfer-Based Recognition of Membrane Cholesterol by Controlling Intradistance of Linker

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Abstract: Gold nanoparticles (AuNPs) are good candidates for donor material in energy transfer systems and can easily be functionalized with various ligands on the surface with Au–S bonding. Cyclodextrin (CD) forms inclusion complexes with fluorophores due to its unique structure for host–guest interaction. In this study, we fabricated βCD-functionalized AuNPs using different lengths of thiol ligands and recognized cholesterol to confirm the energy-transfer-based turn-on fluorescence mechanism. AuNP–βCD conjugated with various thiol ligands and quenched the fluorescein (Fl) dye, forming βCD-Fl inclusion complexes. As the distance between AuNPs and βCD decreased, the quenching efficiency became higher. The quenched fluorescence was recovered when the cholesterol replaced the Fl because of the stronger binding affinity of the cholesterol with βCD. The efficiency of cholesterol recognition was also affected by the energy transfer effect because the shorter βCD ligand had a higher fluorescence recovery. Furthermore, we fabricated a liposome with cholesterol embedded in the lipid bilayer membrane to mimic the cholesterol coexisting with lipids in human serum. These cellular cholesterols accelerated the replacement of the Fl molecules, resulting in a fluorescence recovery higher than that of pure lipid. These discoveries are expected to give guidance towards cholesterol sensors or energy-transfer-based biosensors using AuNPs.

Keywords: cyclodextrin; host-guest interaction; gold nanoparticle quenching; surface modification; turn-on sensing

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1. Introduction

Gold nanoparticles (AuNPs) have been widely used in bioapplications because of their useful properties, such as size- and shape-dependent optoelectronics [1,2], simple and multi-functionalization [3], plasmonic effect [4], good biocompatibility [5,6], and low toxicity [7]. The surface chemistry of AuNPs is crucial in functionalizing various ligands on their surface [8–11]. To use the specific Au–S bond with a thiolated ligand or thiol functional group, AuNPs can be functionalized with various bioligands, such as DNA [12,13], peptide [14], antibody [15], antigen [16], lipid [17], and enzyme [18]. Additionally, AuNPs are good candidates as donor materials due to their good quenching efficiency in a wide range of wavelengths in the visible light area for energy transfer [19–21]. According to Föster's theory, the rate of energy transfer is considerably affected by the distance between the donor and acceptor [22–25].

Cyclodextrin (CD) is an oligosaccharide consisting of a cyclic ring structure of glucose subunits. It has three different sizes of ring structures depending on the number of glucoses: six for α-cyclodextrin (αCD), seven for β-cyclodextrin (βCD), and eight for γ-cyclodextrin (γCD). It can form inclusion complexes with various molecules, known as host–gust interaction, due to its unique structure with a hydrophobic cavity and hydrophilic outside [26]. Depending on the type of CD or modification of functional groups, binding affinity with