Developing Multifunctional Nanoparticles *via* Host-Guest Interactions for Imaging, Delivery and Targeting in Cancer Therapy

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Introduction

Multifunctional nanoparticles harboring various functions including targeting, imaging, and therapy have been intensively studied for application in early detection and treatment of human cancer. Recently, multifunctional groups have been covalently conjugated to smart polymers for a diagnostic therapy.[1] However, the covalent synthetic steps are often complicated and time-consuming.

In this work, we report multifunctional particles *via* host-guest interactions responding to a request. Host-guest interactions were used here as a mild and easy conjugation method.[2] As a model system on demand, branched polyethyleneimine (PEI) was selected as scaffold polymer and β-CD were conjugated as the host units. PEI-CD was synthesized and decorated with a model imaging probe FITC-conjugated adamantine (AD-FITC) and targeting molecule galactose-conjugated PEG-azobenzene (Az-PEG-LA)by simple mixing in aqueous solution.

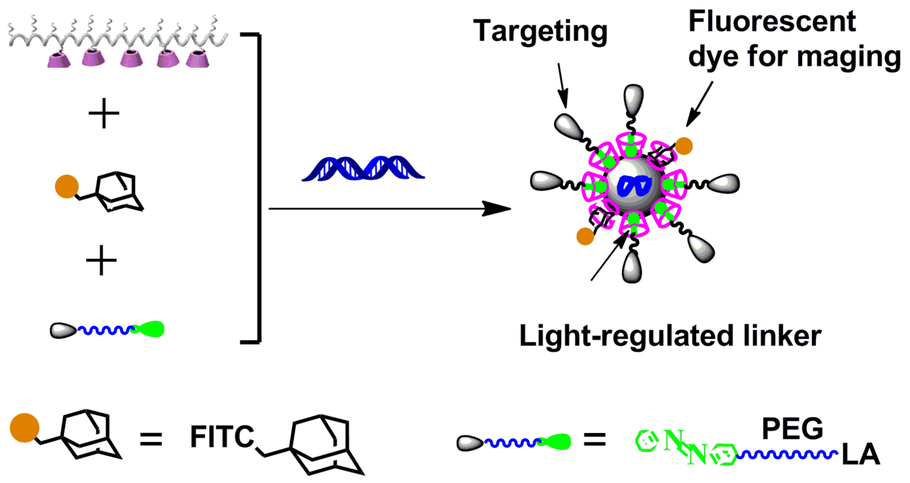

Fig. 1 Illustration of the multifunctional nanoparticles developed via host-guest interaction for imaging, targeting and delivery in cancer therapy.

Results & Discussion

Characterization of model system of nanoparticles

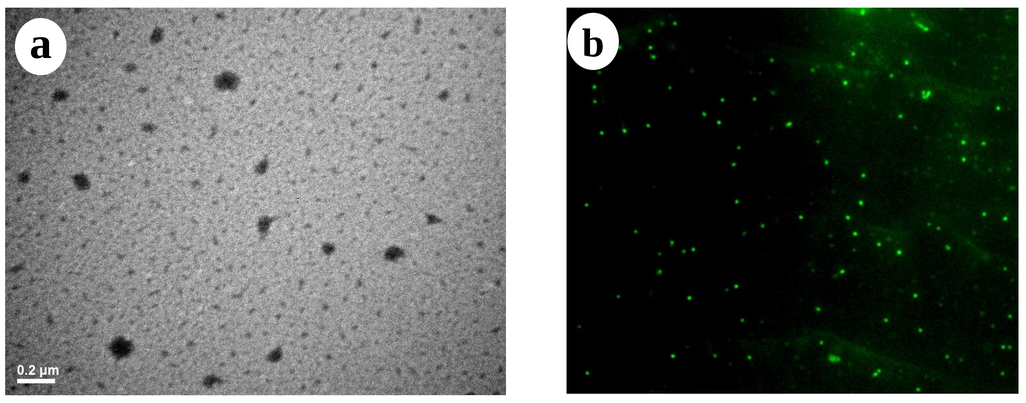

Fig. 2 TEM (a) and fluorescence (b) images of PEI-CD/AD-FITC/Az-PEG-LA/DNA particles (N/P=10) .

➢ **Fluorescent particles with diameter of below 100 nm were could be successfully prepared *via* host-guest interactions.**

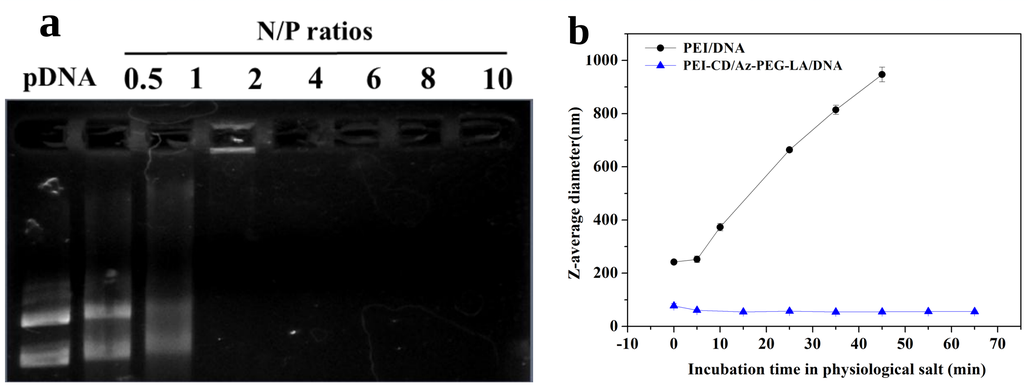

Fig. 3 Agarose gel electrophoresis retardation PEI-CD/AD-FITC/Az-PEG-LA/DNA particles (a) . Diameters of the particles in 150 mM NaCl at N/P ratio of 10 (b) .

➢**Multifunctional particles via host-guest interactions had little influence on the DNA binding ability, and the particles had good stability under physiological salt conditions.**

Target-specific cellular uptake of the nanoparticles

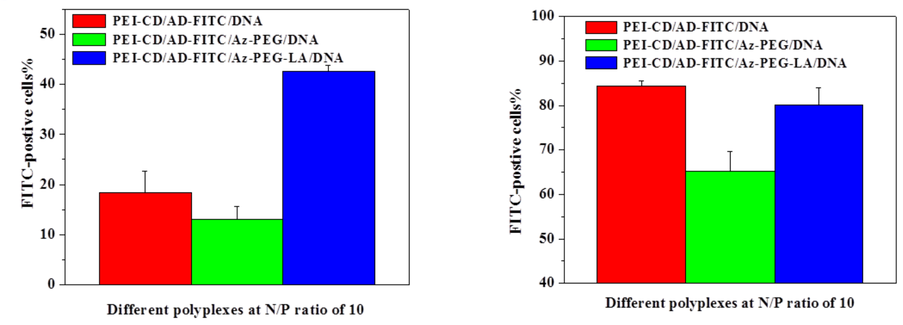

Fig. 4 Cellular uptake by HepG2 cells (cancer cells) for 0.5 h (a) and 4.5 h (b).

➢ **Multifunctional particles showed higher cellular uptake efficiency than PEGylated particles without target molecules.**

Bioimaging for target-specific intracellular delivery

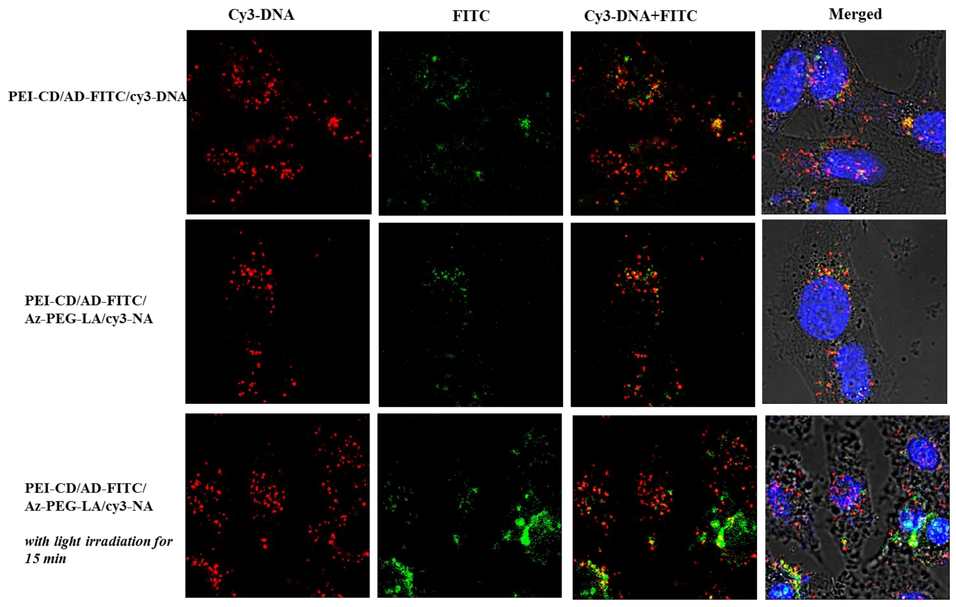

Fig. 5 CLSM images of cells exposed to different polymers complexed with cy3-DNA (Red) for 4.5 h incubation and incubated for another 12 h. DAPI stained the cell nuclei (blue).

➢ **The multifunctional particles with bright fluorescence signal was detected, and light stimuli enabled DNA release.**

Gene expression of the multifunctional nanoparticles

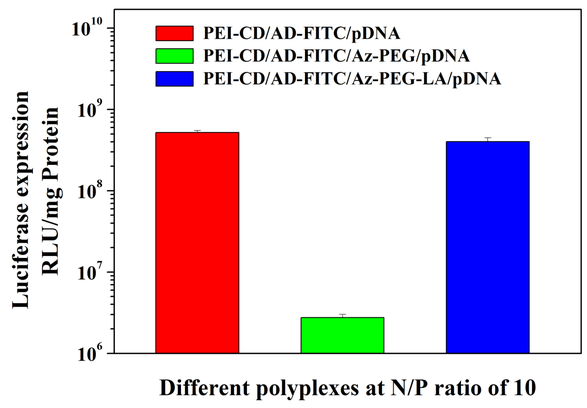

Fig. 6 *In vitro* transfection of the luciferase gene by HepG2 cells with different nanoparticles.

➢**The therapeutic signal of luciferase had similar level with that of PEI/pDNA particles, higher than that of nanoparticles without target molecules.**

Conclusion

Multifunctional nanoparticles on demand were successfully developed by host-guest interactions between β-cyclodextrin and its guest molecules. As a model system on demand, PEI-CD/AD-FITC/Az-PEG-LA particles had good salt stability, were applied to the bioimaging of its targeted delivery to HepG2 cells and its therapeutic signal of luciferase had similar level with that of PEI/pDNA particles. The multifunctional nanoparticles developed via host-guest interactions can be exploited as a platform technology for various bioimaging, targeting, delivery, and tissue engineering applications.

References

1. M. A. C. Stuart, I . Luzinov, et al. *Nat Mater* 2010, 9, 101-113.
2. W.Y. Li, Y.X. Wang, et al. *Chem Commun* 2012, 48, 10126-10128.

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