

Construction of OligoDNA-Based Nanoparticles Self-Assembled from OligoDNA-Poly(carbamate) Conjugates

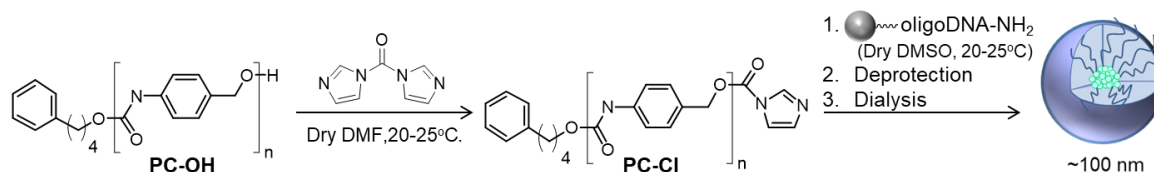
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Introduction

Nanoparticles covered with a high density of oligomeric nucleic acids (oligoDNA) have emerged as a promising tool for nucleic acid delivery because of highly efficient cellular uptake and enhancement of resistance to nuclease degradation.[1] To construct this nanostructure, gold nanoparticles without degradation properties are generally adapted as a core material.[2] However, there remain a concern about precise control of nucleic acid release in safe intracellular delivery. Here, we describe preparation of oligoDNA-based nanoparticles containing a core structure of self-immolative poly(carbamate) (PC) though the solid-phase technique.

Experimental

To obtain a conjugation of PC derivatives with oligoDNA (PC-oligoDNA), PC possessing a hydroxy group (PC-OH, degree of polymerization: 2) [3] was treated with *N,N'*-carbonyldiimidazole in dry DMF at 20-25°C for 3h to offer PC derivatives with carbonylimidazole moiety (PC-CI) as a white powder (**Scheme 1**). PC-CI thus obtained was conjugated with amine-terminated 17 nucleotide (nt) oligoDNA on a solid support in DMSO at 20-25°C for 24 h to give PC-oligoDNA. Subsequently, *in situ* self-assembled nanoparticles were carried out using dialysis (MWCO:1,000) against water overnight. Particle size and zeta potential were measured by dynamic light scattering (DLS) and electrophoretic light scattering, respectively.



Scheme 1. Preparation of self-assembled nanoparticles composed of a dense DNA shell surrounding a self-immolative PC derivatives core.

Results and Discussion

PC derivatives possessing aminobenzyl alcohol as a repeating unit can cause self-immolative degradation through 1,6-elimination and decarboxylation reactions. PC-OH having a such property gave end-activated PC-CI in 30% yield. The conversion of the hydroxy group to the CI moiety was confirmed to be 76% from ¹H-NMR spectrum. Conjugation of PC-CI with 17-nt oligoDNA on the solid support and subsequent *in situ* self-assembly of PC-oligoDNA conjugates were then performed. The DLS measurements revealed that the hydrodynamic diameter and polydispersity index (PDI) were 107 nm and 0.085, respectively.[4] Additionally, after incubation for one day, the nanoparticles in the solution showed a similar hydrodynamic diameter (=107 nm) and PDI (=0.085). Furthermore, the zeta potential of the nanostructures was found to be -34.5 mV, which is consistent with that of gold nanoparticles modified with negatively charged DNA.[5] These results demonstrate the forma of a nanoparticle covered with a dense DNA shell in an aqueous solution.

References

[1] J. I. Cutler *et al.*, *J. Am. Chem. Soc.*, **2012**, *134*, 1376. [2] N. L. Rosi *et al.*, *Science*, **2006**, *312*, 1027. [3] A. Sagi *et al.*, *J. Am. Chem. Soc.*, **2008**, *130*, 5434. [4] S. Fukumoto *et al.*, *Anal. Sci.* **2021**, *37*, 781. [5] A. Barchanski *et al.*, *Bioconjugate Chem.* **2012**, *23*, 908.

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