

# Studies on Well-Defined Nano-Complexes Derived from Stimuli-Responsive Polymers

Yumi KUBOSHIMA

## 1. Introduction

Recently, stimuli-responsive polymers have attracted much attention as the component for micelle or associates-forming block copolymers. Because the resulting stimuli-responsive polymeric micelles become a candidate to fabricate the novel drug delivery systems with higher potentials. Actually temperature-responsive polymeric micelles can be easily derived from poly(N-isopropylacrylamide) (abbreviated as PIPAAm)-based block copolymers with hydrophobic segment. Anyway, complex formation of polyions is also practical as the driving force for another unique polymeric micelles or associates. The polyion complex micelles are formed by the electrostatic interactions between oppositely charged block copolymers in aqueous solutions. The ionic block copolymers with polyethylene oxide segment exhibit self-assemble behaviors exclusively.

In this study, we prepared the nano-complexes derived from ionic stimuli-responsive block copolymers with carboxyl groups and poly(amidoamine) dendrimers with amino groups by the electrostatic interactions and characterized them in the aqueous media. The stimuli-responsive block copolymers consist of two segments, PIPAAm and poly(methacrylic acid) (abbreviated as PMAA) and formed the AB- or ABA-type block copolymers. Furthermore, the effective nano-complex stabilization was carried out by the condensation reactions between the block copolymers and the dendrimers.

## 2. Results and Discussions

PNIPAAm-b-PMAA as AB-type diblock copolymer and PMAA-b-PNIPAAm-b-PMAA as ABA-type

triblock copolymer were prepared by hydrolysis of corresponding precursors, PNIPAAm-b-t-butyl methacrylate (t-BMA) and t-BMA-b-PNIPAAm-b-t-BMA. They were synthesized by atom transfer radical polymerization (ATRP) according to the literature. The block copolymers were dissolved in 50 mM tris HCl buffer solutions at a concentration of 1.0 mg/mL with adjusted pH. Then, the PAMAM dendrimer solution described above was added to the block copolymer solutions with stirring.

Interestingly, the sizes of the complexes obtained were different depending on the types of starting block copolymers. The nano-complexes derived from ABA-type block copolymer had smaller size than that from diblock copolymers. It might be due to the difference in the complex formation process.

Next we investigated the improvement of the complex stability by chemical reaction. After the reaction, as expected, the both solutions have maintained similar properties and the nano-sized complexes could not dissociate even though it was exposed at pH = 13. Obviously, the amide bonding formation contributed to improve the stability in severe condition.

We examined the thermo-responsive profiles of prepared nano-complexes in aqueous solutions by turbidity measurements. The nano-complexes with and without stabilization shows the sensitive responsive behavior.

## 3. Conclusions

The polymer modification with stimuli-response in this study can surely contribute to the bio-conjugate chemistry and drug delivery system because of not only the easy preparation but also the size control of the complexes.