ABSTRACT

This dissertation describes the two types of stimuli-responsive gene carriers, in which supramolecular structured cationic polymers. These cationic polymers were designed to be dissociated by the protonation of linear polymeric chain or the reduction of terminal disulfide moieties in a low pH or reductive environment, respectively. First one is a polypseudorotaxane consisting of a linear polyethylenimine with *M*n of 22000 (LPEI22k) and γ-cyclodextrins (γ-CDs) (LPEI22k/γ-CD) was examined as a gene carrier. Second is a biocleavable polyrotaxane, in which necklace-like structure between many cationic α-cyclodextrins (α-CDs) and a disulfide-introduced poly(ethylene glycol) (PEG) (DMAE-SS-PRX).

LPEI22k/γ-CD formed pDNA polyplex at higher N/P ratio than LPEI22k, suggesting the γ-CD threading sterically decreased the cation charge density of LPEI22k. The decreased cation charge density of polyplex by γ-CD threading may prevent the interaction between secondary amines of LPEI22k and cell membranes, resulting in high cell viability even at higher N/P ratio. Furthermore, transfection efficiency of LPEI22k/γ-CD at N/P 50 showed over 120-fold higher than LPEI22k, although the transfection efficiency at N/P 10 and 20 were almost the same with the others. These results are likely to γ-CDs in LPEI22k/γ-CD hindered the interaction between secondary

amines in LPEI22k and cell membranes, resulting in significant transfection efficiency via reduction of cytotoxicity even at higher N/P ratio.

On the other hand, DMAE-SS-PRX showed the stable polyplex formation and stimuli-responsive pDNA decondensation (pDNA release) via the dissociation of the mechanical linkages between α-CDs and PEG. The stable polyplex was formed by mixing very small amount of the DMAE-SS-PRX with pDNA, which is likely to be due to the mobile motion of α-CDs in the necklace-like structure of the DMAE-SS-PRX. In addition, the pDNA decondensation of the polyplex occurred through disulfide cleavage of the DMAE-SS-PRX and subsequent α-CD release, which significantly improved transfection efficiency and cell viability.

Key words: **Non-viral gene vector, supramolecular structure, polyrotaxane, polypseudorotaxane, stimuli-responsive gene carrier**