# Supporting information

## siRNA-Loaded Polyion Complex Micelle Decorated with Charge-Conversional Polymer Tuned to Undergo Stepwise Response to Intra-Tumoral and Intra-Endosomal pHs for Exerting Enhanced RNAi Efficacy

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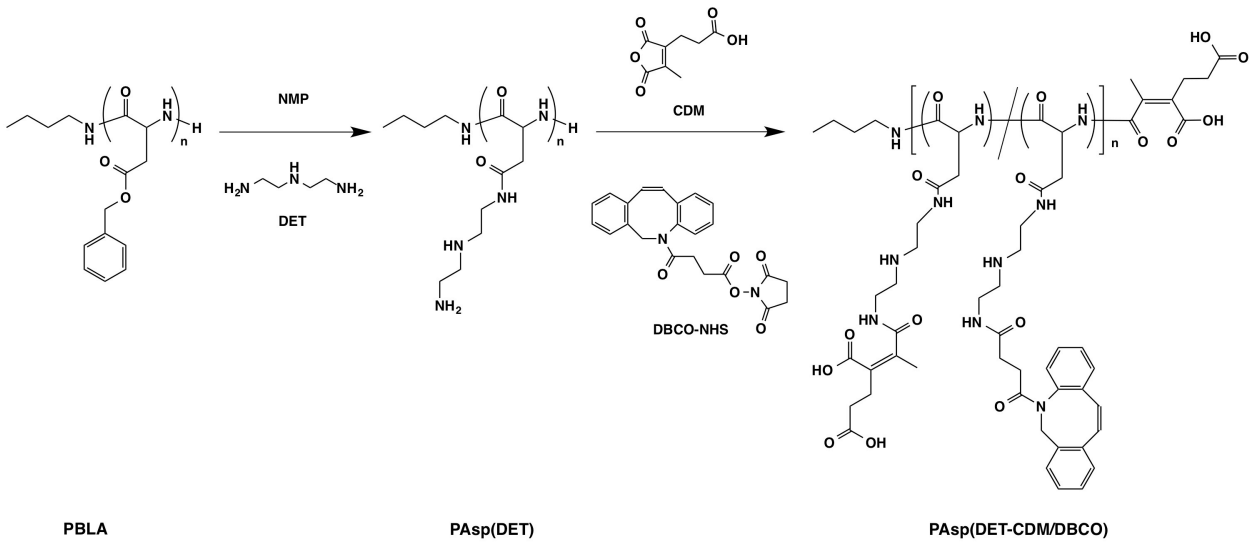


**Scheme S1.** Synthesis procedure of PAsp(DET-CDM/DBCO). This polyaspartamide derivative has the mixed sequence of α and β isomers and its ω-end may be modified with either CDM or DBCO moieties. The α isomers of PAsp(DET) and PAsp(DET-CDM/DBCO) and the CDM-modified ω-end are depicted as a representative structure for simplicity.

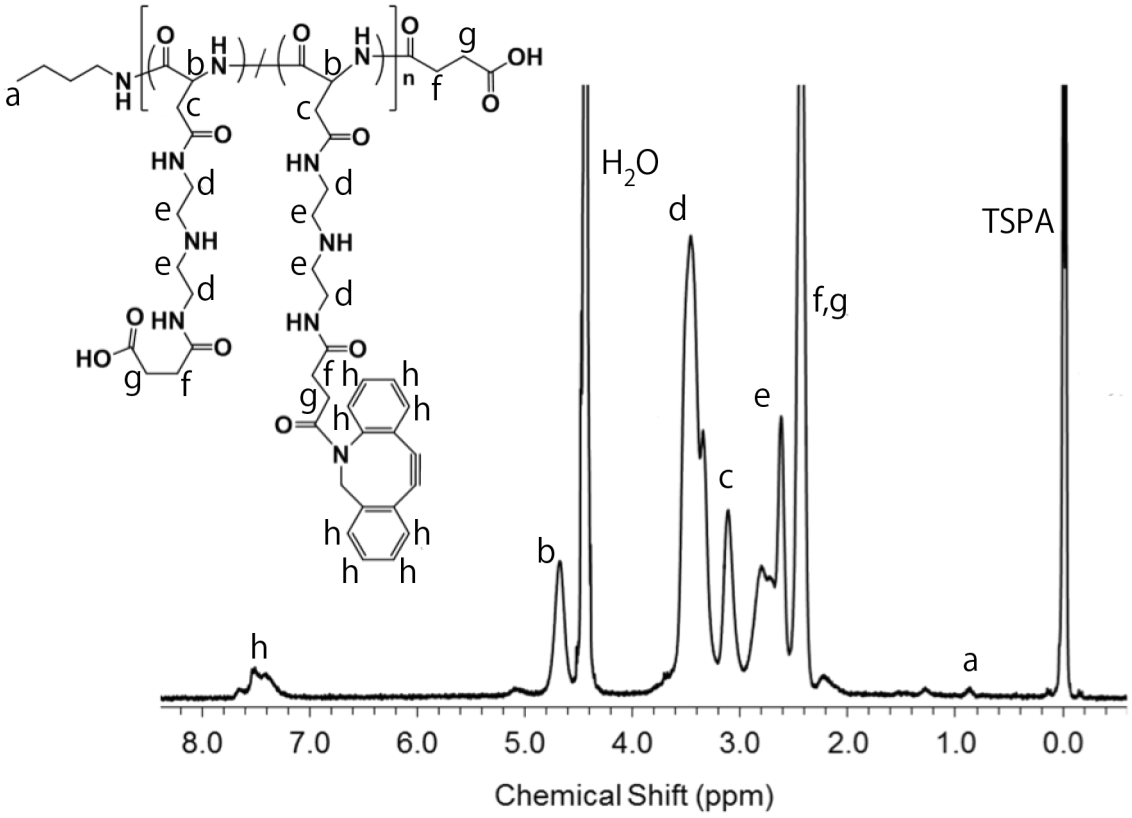


**Figure S1.** $^{1}$H NMR spectrum of PAsp(DET-SUC/DBCO) in $D_2O$ at 70 ºC (polymer concentration = 5 mg/mL). This polyaspartamide derivative has the mixed sequence of α and β isomers and its ω-end may be modified with either SUC or DBCO moieties. Only α isomer of PAsp(DET-SUC/DBCO) and SUC-modified ω-end are depicted as a representative structure for simplicity.

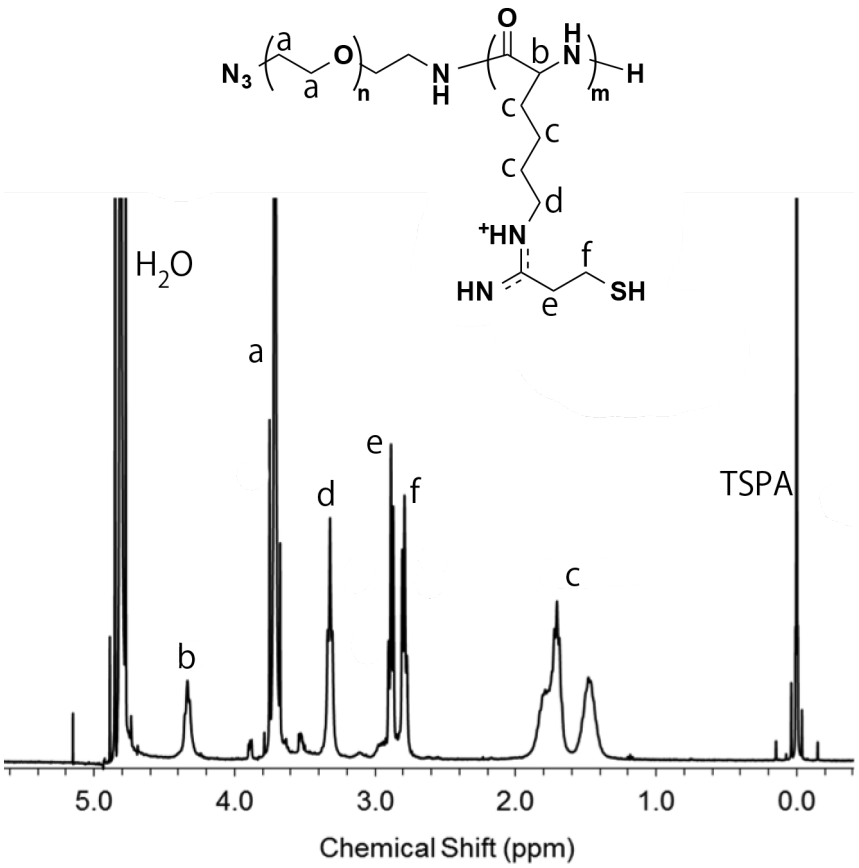


**Figure S2.** $^{1}$H NMR spectrum of $N_3$-PEG-*b*-PLys(MPA) in $D_2O$ at 25 ºC (polymer concentration = 5 mg/mL).

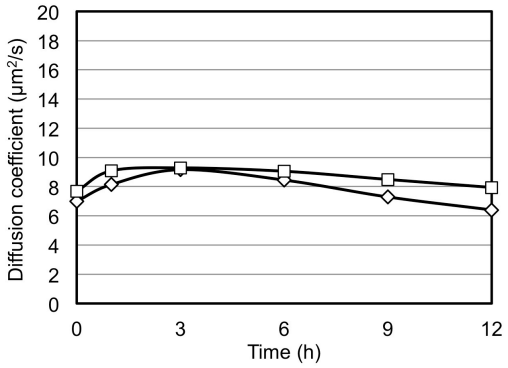


**Figure S3.** Stability of nonmodified micelles (open diamond) and CDM-micelles (open square) (100 nM Cy3/Chol-siRNA) in 90% FBS-containing HEPES buffer (pH 7.4), determined by FCS.

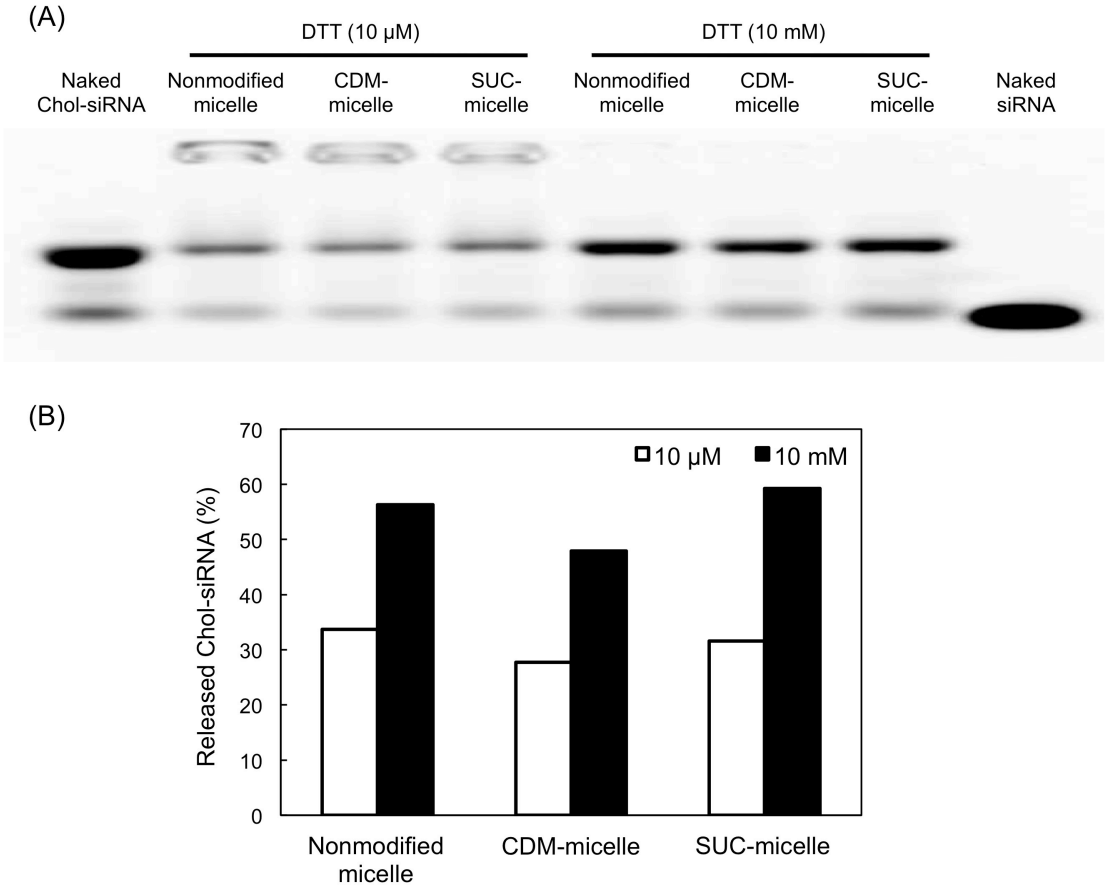


**Figure S4.** siRNA release profiles of nonmodified micelle, CDM-micelle, and SUC-micelle under two varying reductive conditions. Each micelle sample was prepared with Cy3/Chol-siRNA and mixed with dextran sulfate at a residual molar ratio of sulfate group in dextran sulfate to phosphate group in siRNA = 0.5 in the presence of 10 μM or 10 mM concentration of dithiothreitol (DTT). After 1 h incubation at 37 ºC, samples were electrophoresed in 1% agarose gel (100 V, 20 min). The agarose gel was imaged (A) and quantitatively analyzed based on densitometry of detected Cy3 signals (B) using Molecular Imager® PharosFX$^{TM}$ Systems (Bio-Rad Laboratories).

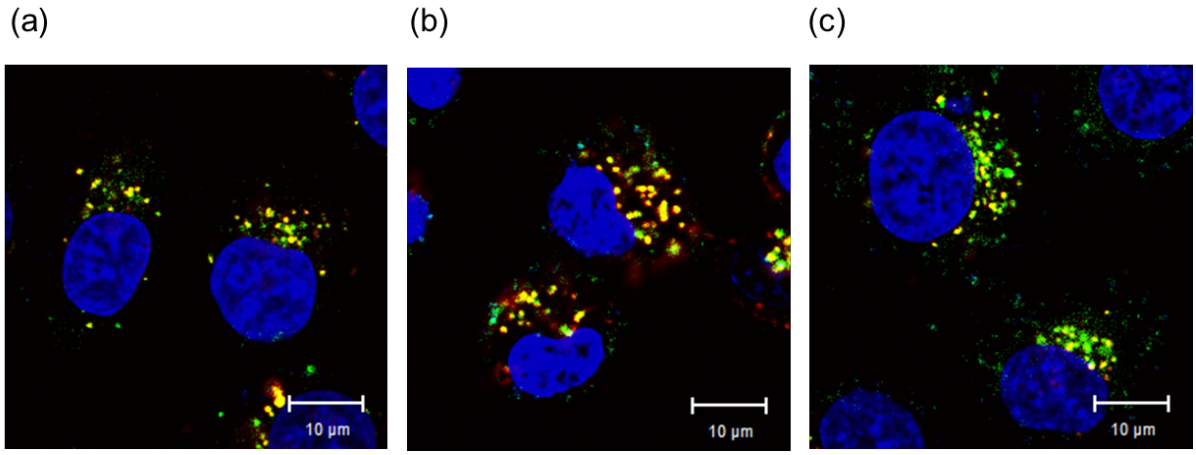


**Figure S5.** CLSM images of A549 cells after 12 h incubation with (a) nonmodified micelles, (b) CDM-micelles, and (c) SUC-micelles at pH 6.7 (siRNA concentration = 200 nM). Red: Cy3/Chol-siRNA, green: late endosome/lysosome stained with LysoTracker Green, blue: nuclei stained with Hoechst 33342, and yellow: colocalization between red and green pixels.

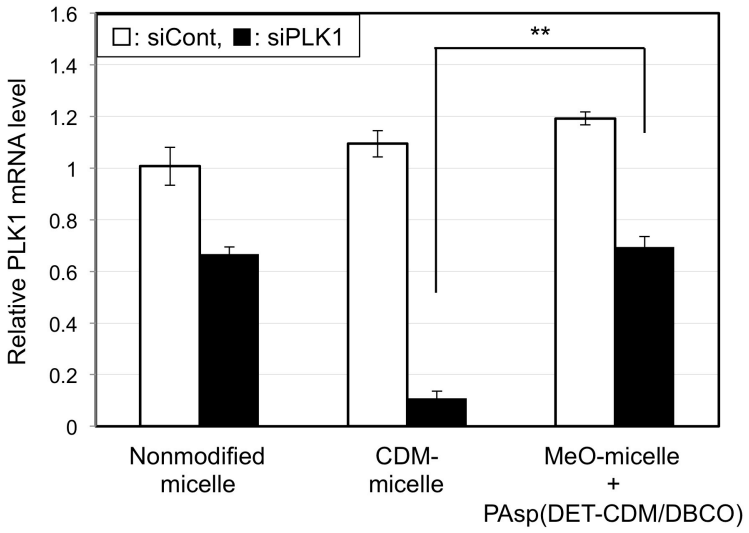


**Figure S6.** Gene silencing efficiencies of nonmodified micelles prepared from $N_3$-PEG-*b*-PLys(MPA) without PAsp(DET-CDM/DBCO), CDM-micelles prepared from $N_3$-PEG-*b*-PLys(MPA) with PAsp(DET-CDM/DBCO), and MeO-micelles prepared from MeO-PEG-*b*-PLys(MPA) with PAsp(DET-CDM/DBCO) in A549 cells cultured at pH 6.7 (siRNA concentration = 200 nM). Data represent the means ± SEM (n = 4). **: $p < 0.01$.

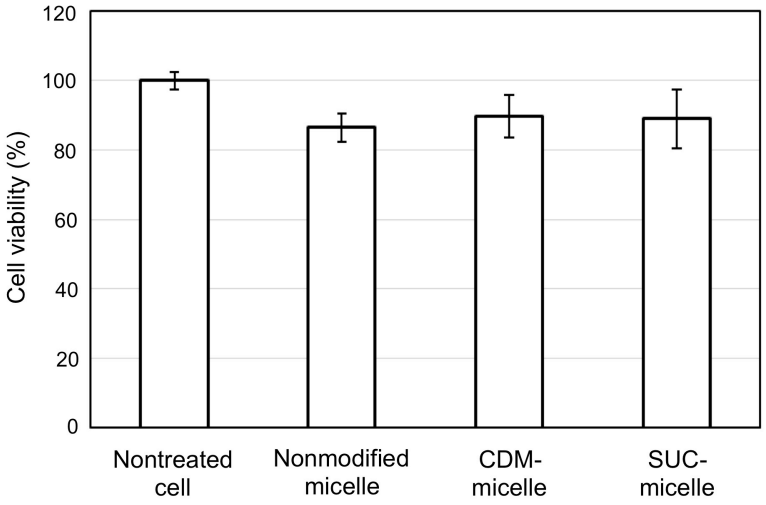


**Figure S7.** Viability of A549 cells after 48 h incubation with nonmodified micelles, CDM-micelles, and SUC-micelles at pH 7.4 (siRNA concentration = 200 nM). Data represent the means ± SEM (n = 4).