Supporting Information

Cell-penetrating poly(disulfide)s-based star polymer for simultaneous intracellular delivery of miRNAs and small molecule drugs

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Additional Supporting Video

Supplementary Video: 3D projection of HeLa cells incubated with βCD-CPD-miR-203^{Cy5} (10 μM) for 2 h and the stained with LysoTracker^{TM} Green (green) and Hoechst (blue).

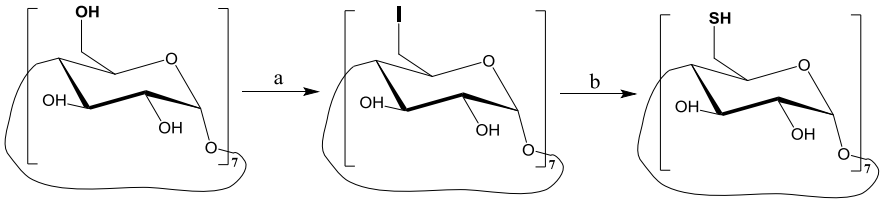


Figure S1. Synthetic schemes for the synthesis of βCD-SH. Conditions: **a**) β-Cyclodextrin, triphenylphosphane, iodine, DMF, 15 h, 80 ℃, 88%; **b**) thiourea, NaOH, $KHSO_4$, DMF, 20 h, 70 ℃, 85%.

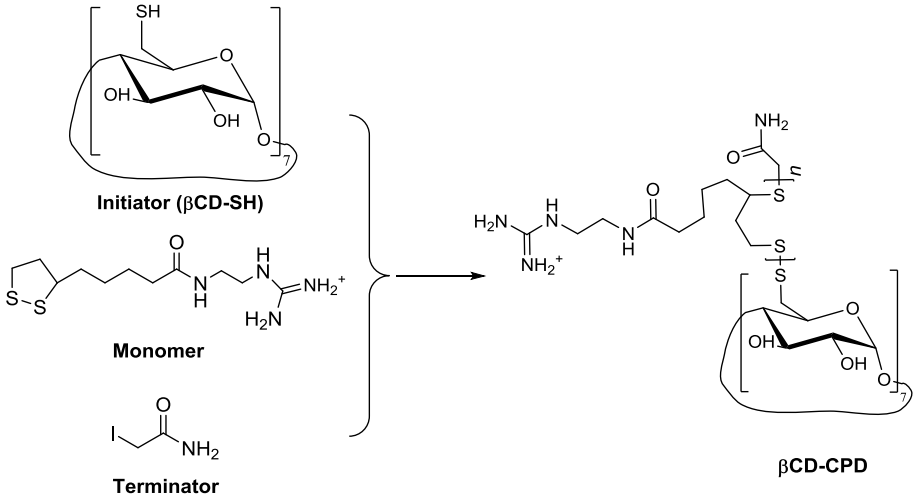


Figure S2. Structure and synthetic schemes of βCD-CPD and the initiator, monomer and terminator used for its synthesis.

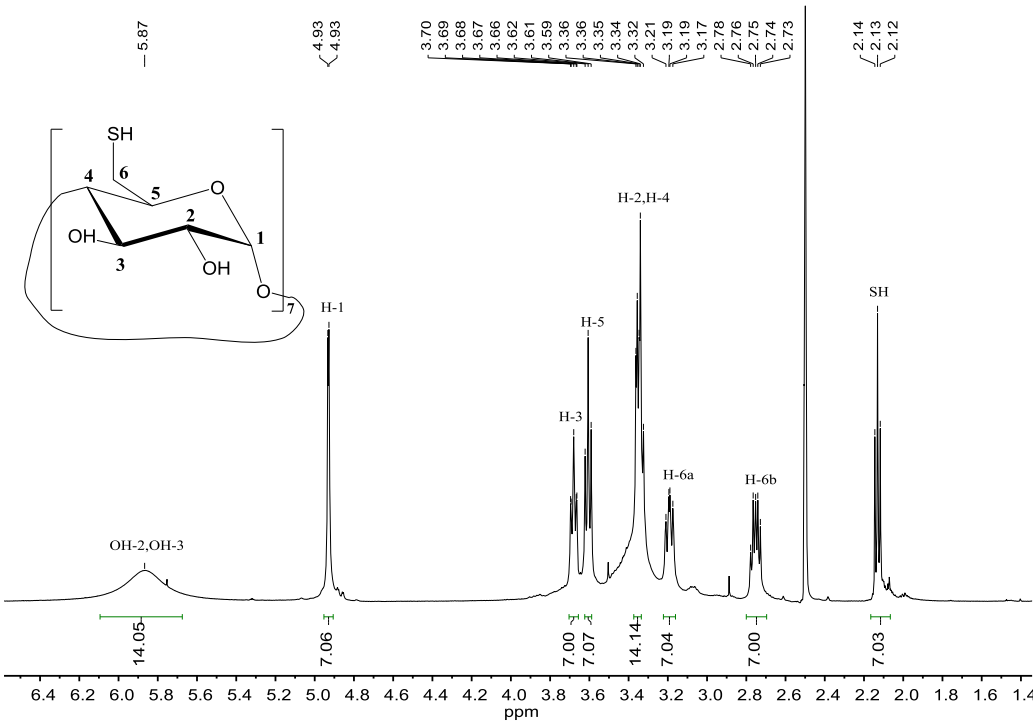
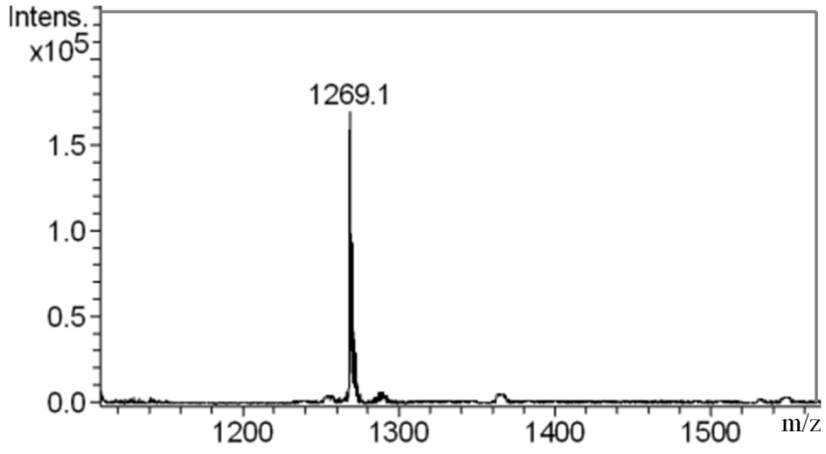


Figure S3. ^{1}H NMR spectrum of βCD-SH (DMSO-d_6).



#	m/z	I	I %
1	1269.1	169327	100.0
2	1270.1	98113	57.9
3	1271.1	93535	55.2
4	1272.1	41707	24.6
5	1273.1	29210	17.2

Figure S4. Mass spectrum of βCD-SH. MS m/z (positive ion FAB) 1269.1 for $[M+Na]^+$, calcd for ($C_{42}H_7O_{28}S_7$) 1247.1

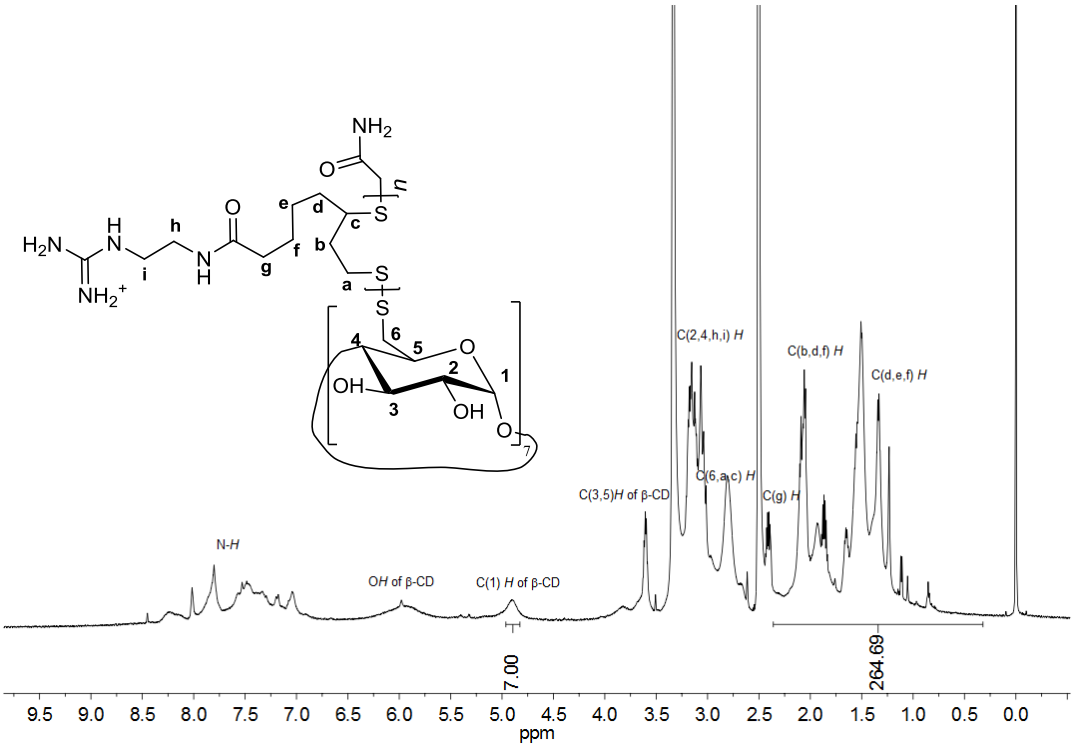


Figure S5. ^{1}H NMR spectrum of βCD-CPD (DMSO-d_6).

The number of guanidinium cation unit on each βCD core is calculated as follows:
As shown in Figure S6, there are 7 protons in the C(1) position for each βCD molecule, and 8 protons in the C(b,d,e,f) position for each monomer unit. Therefore, the number of guanidinium cation unit on each βCD core has been determined to be:

$$n = \frac{264.69/8}{7/7} = 33.1$$

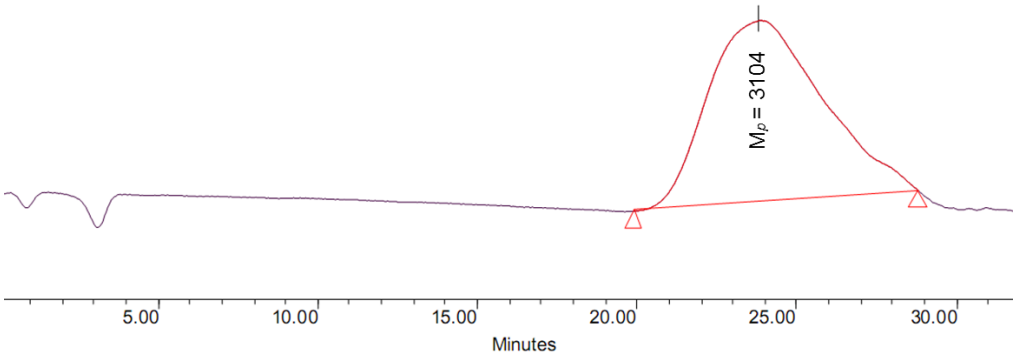


Figure S6. GPC profile of βCD-CPD. The number and weight-averaged molecular weights (M_n = 2.78 ×10^3 and M_w = 3.67 ×10^3) and polydispersity index (PDI = M_w/M_n) of 1.32 were determined by gel permeation chromatography (GPC) equipped with Waters 1515 Isocratic HPLC pump, Waters 2414 Refractive Index Detector, and two Ultrahydrogel^{TM} columns. Elution was 10.0 mM 4-(2-hydroxyethyl)-1-piperazine ethanesulphonic acid (HEPES) buffer at pH 7.4. Elution rate was 0.8 mL min^{-1}. Operation temperature is 40 ℃. A series of poly(ethylene glycol) with M_n ranging from 1000 to 21800 g mol^{-1} were used as standard samples. This value is expectedly smaller than that calculated from ^{1}H NMR, which is 1.09 ×10^4. This is because the mono-dispersed PEG standards used were linear PEG polymers whereas the βCD-CPD polymers were star-shaped. The star-shaped polymer might take up a smaller volume and get trapped inside the column more easily than the linear polymer with the same molecular weight. Therefore, the star-shaped polymers were expected to have a longer retention time which corresponds to a smaller M_n value than the linear polymer with the same molecular weight.

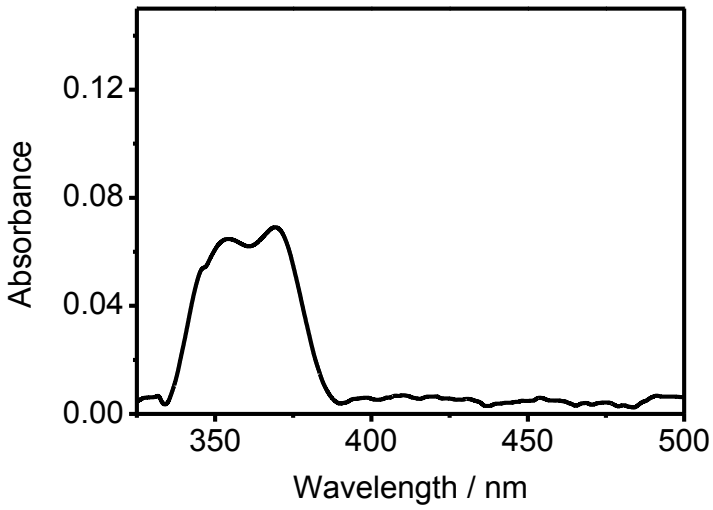


Figure S7. UV-vis absorption spectrum of CPT@βCD-CPD (6.0 μM) in HEPES buffer.

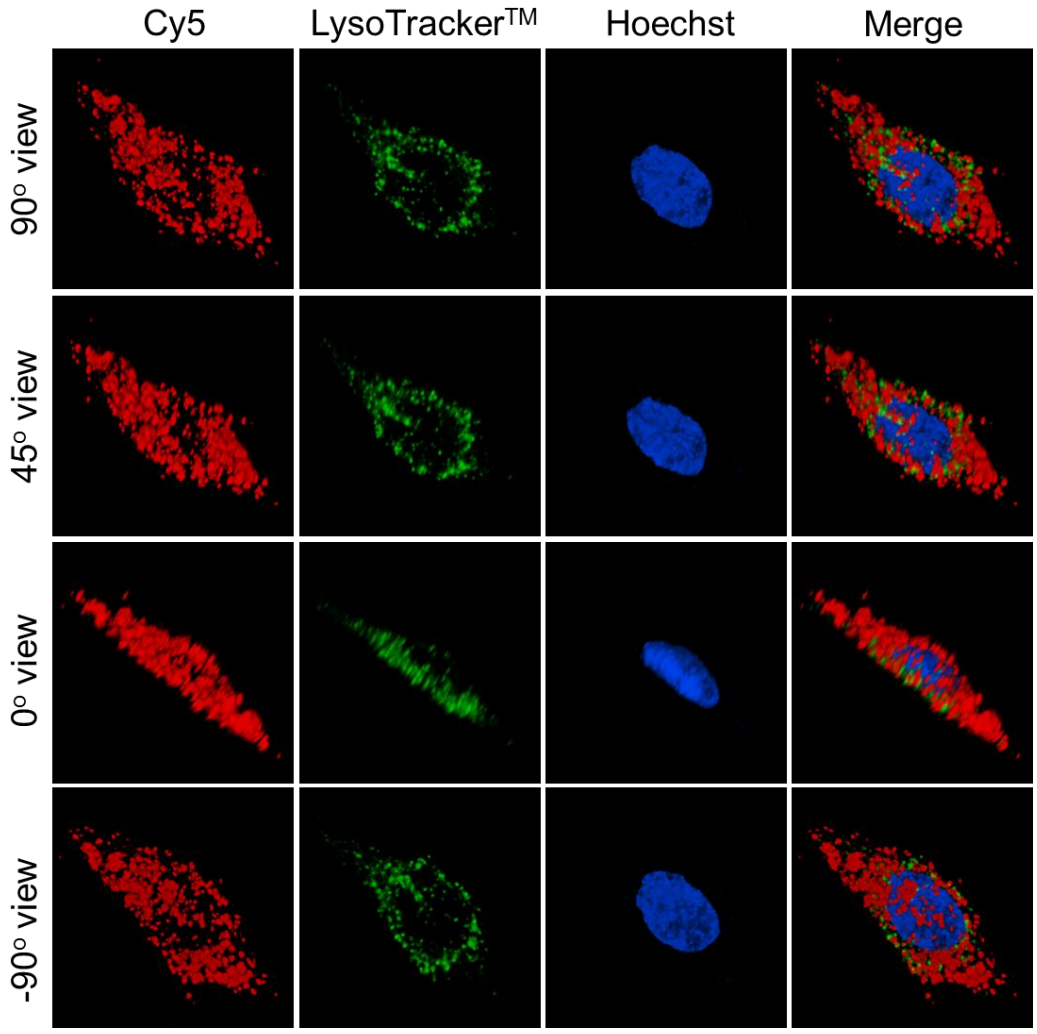


Figure S8. 3D CLSM projections showing *Z*-stack images at different view (step size, 0.163 μm) of HeLa cells incubated with βCD-CPD-miR-203^{Cy5} (10 μM) for 2 h, followed by staining with LysoTracker™ (green) and Hoechst (blue).

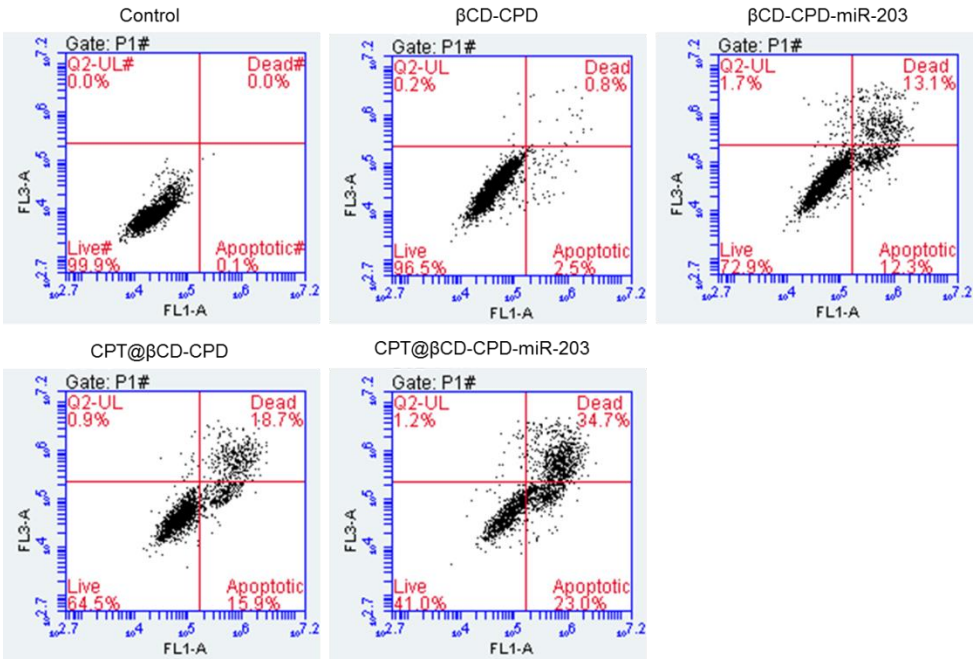


Figure S9. FACS analysis of HeLa cells incubated with different complex (10 μM) for 24 h.

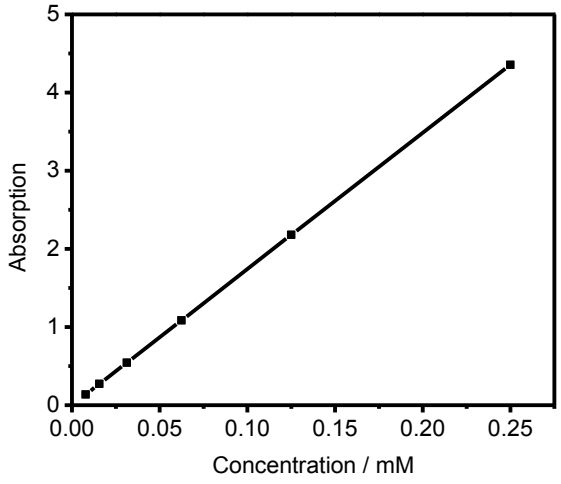


Figure S10. Standard linear calibration curves of CPT UV-vis absorption at 385 nm. It was used for determination of the embedding ratio of CPT.