Supporting Information

Dimeric Prodrug Self-Delivery Nanoparticles with Enhanced Drug Loading and Bioreduction-Responsiveness for Targeted Cancer Therapy

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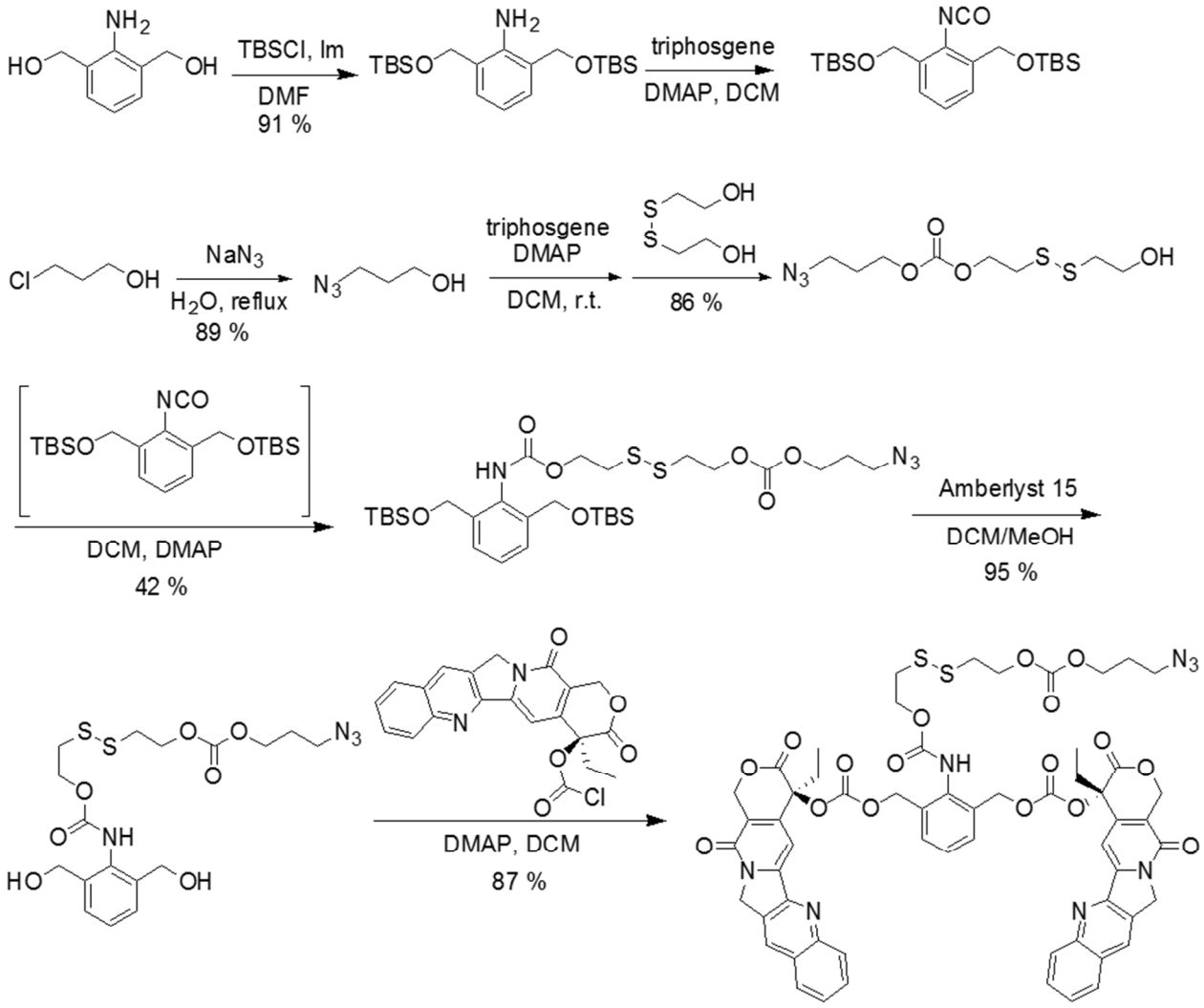
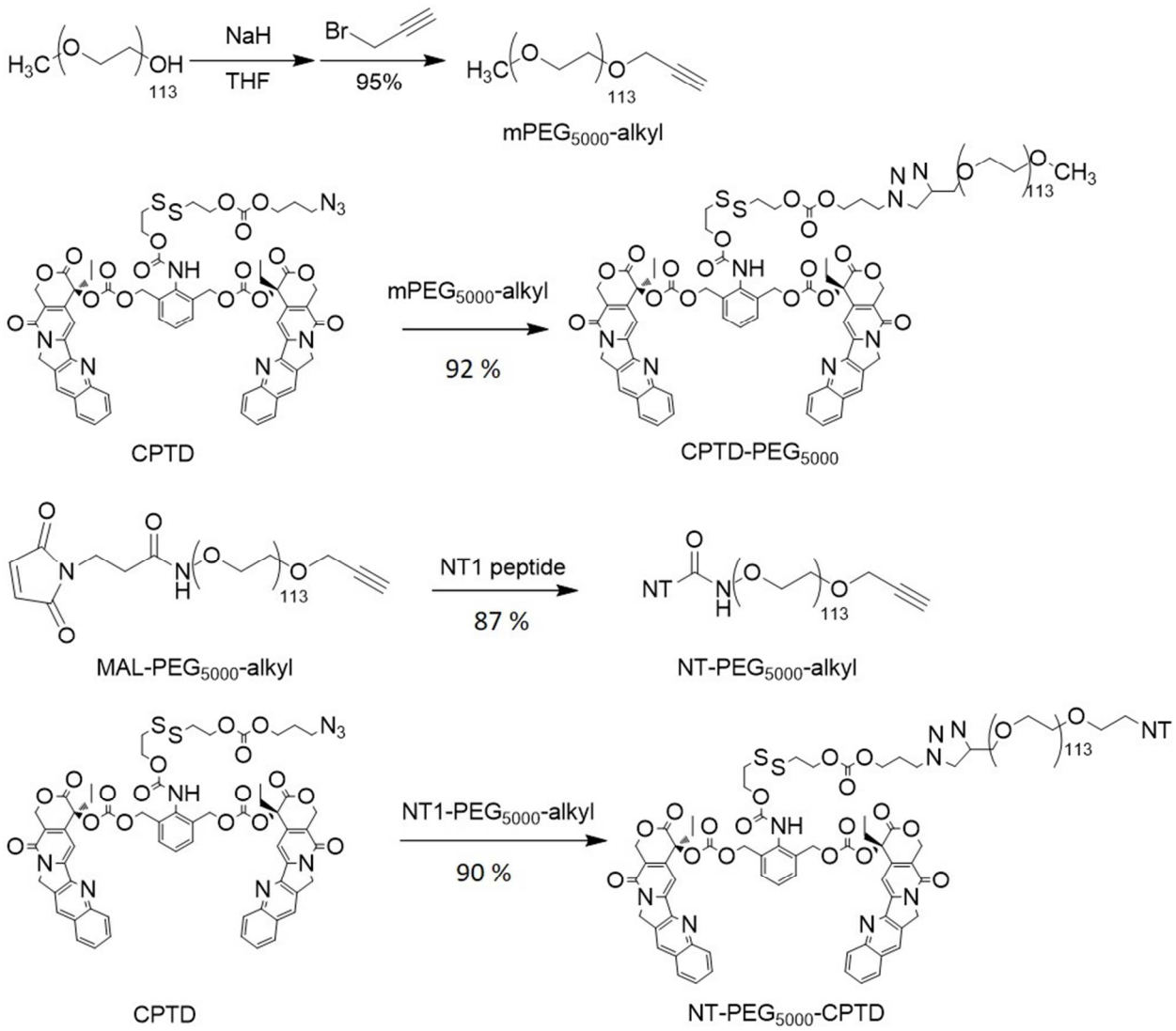
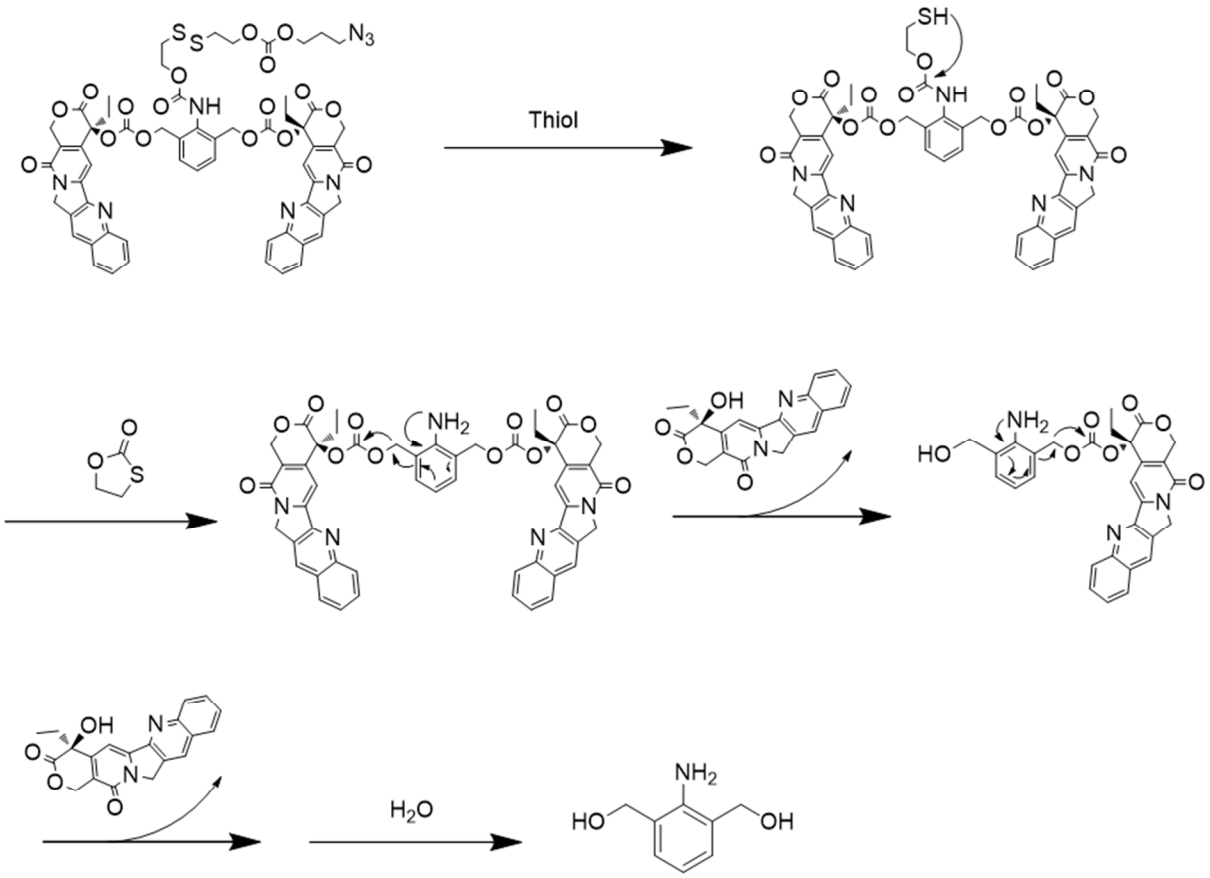


Scheme S1. Synthesis route of CPTD



Scheme S2. Synthesis route of CPTD-PEG_{5000} and NT-PEG_{5000}-CPTD



Scheme S3. Proposed release mechanism of redox-responsive drug release

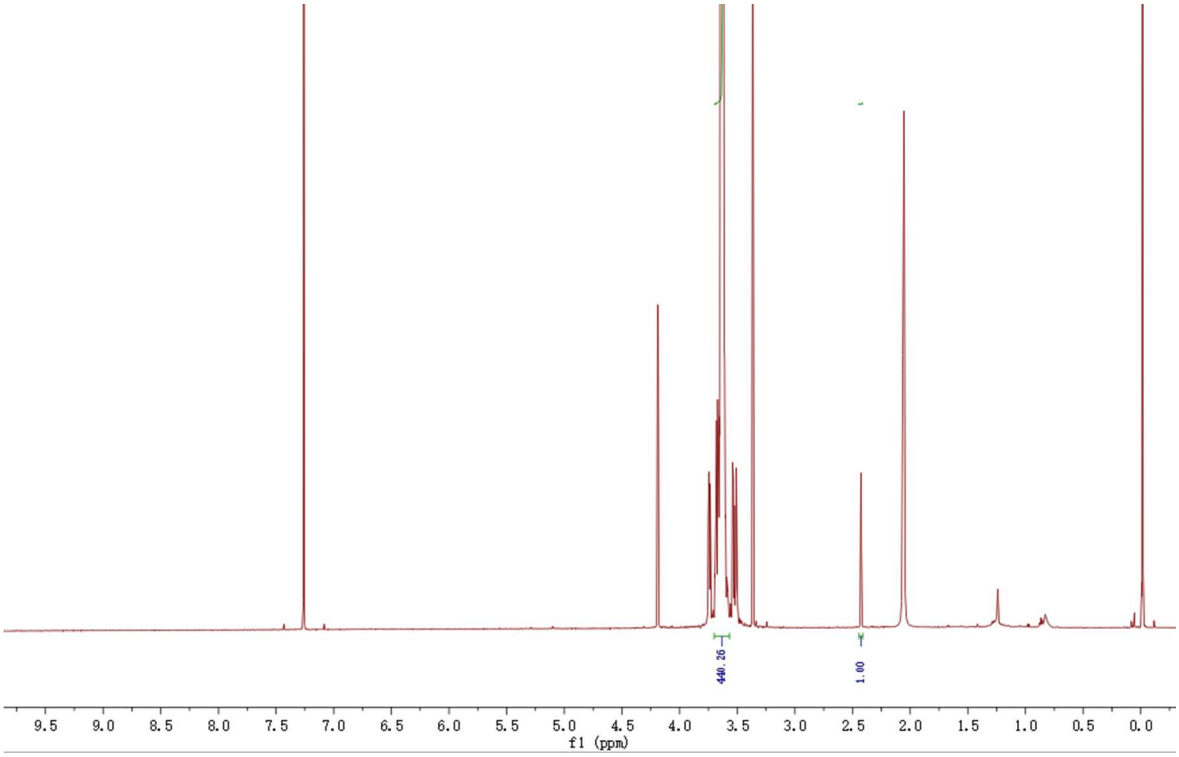


Figure S1. ^{1}H NMR of alkyne-PEG_{5000}

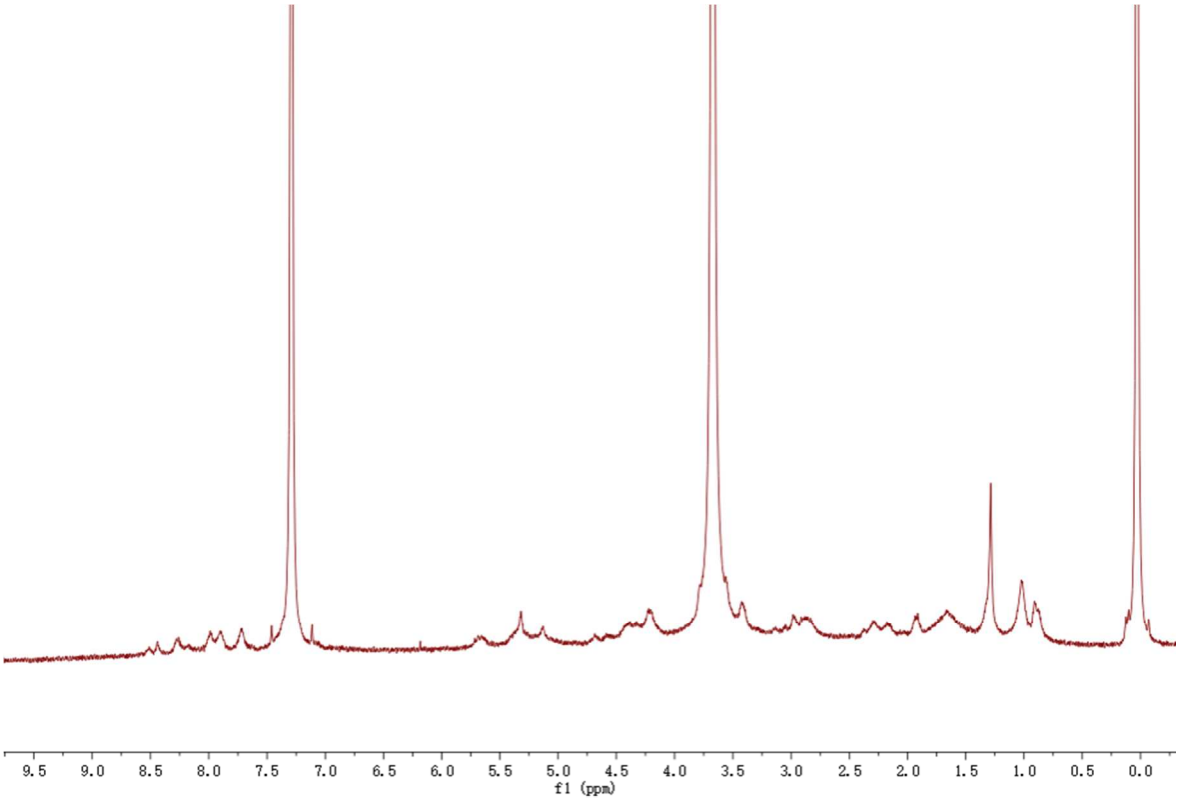


Figure S2. ^{1}H NMR of CPTD-PEG_{5000}

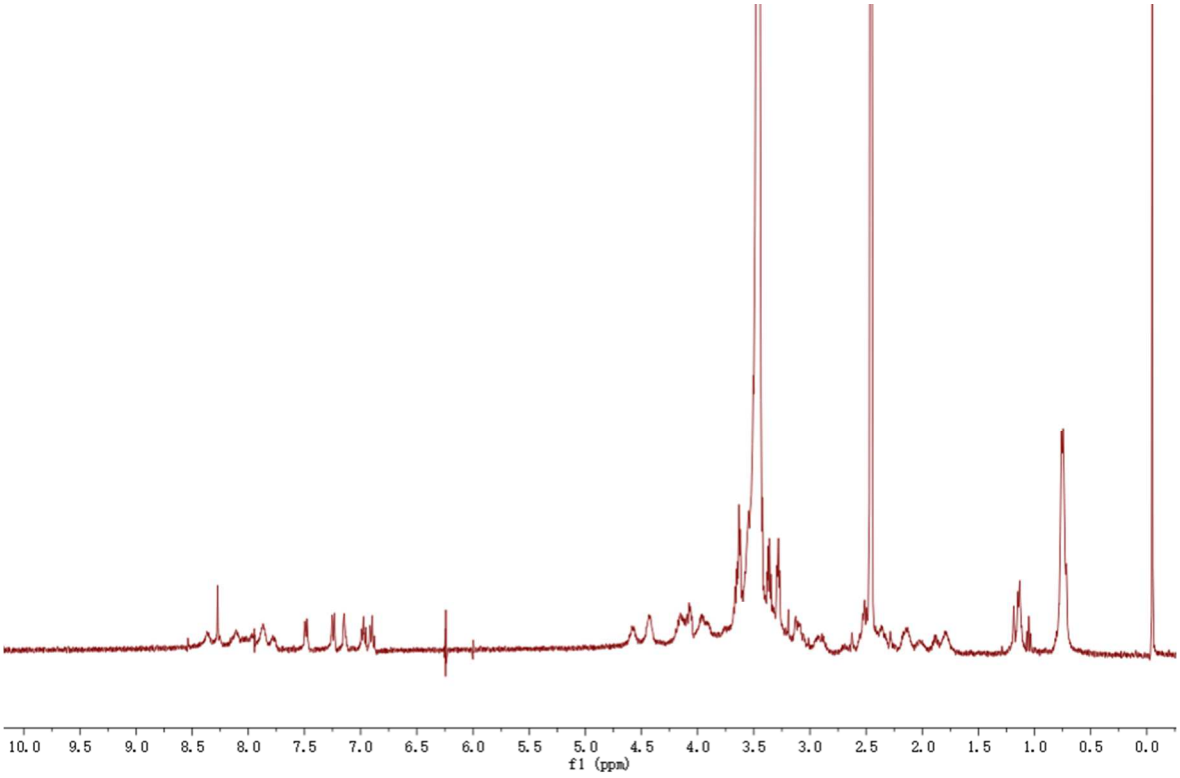


Figure S3. ^{1}H NMR of NT-PEG$_{5000}$-CPTD

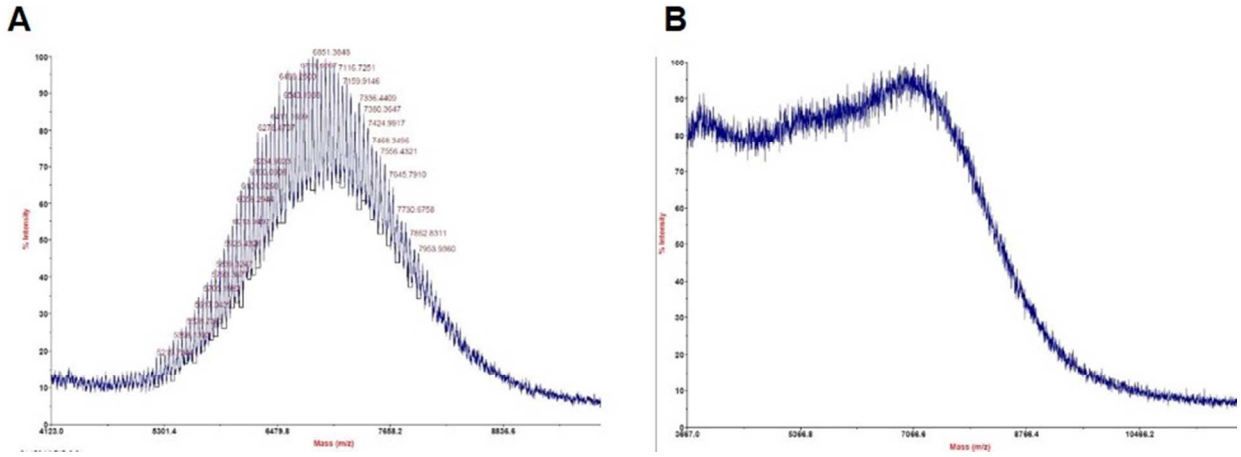


Figure S4. MALDI-TOF of CPTD-PEG$_{5000}$ (A) and NT-PEG$_{5000}$-CPTD (B)

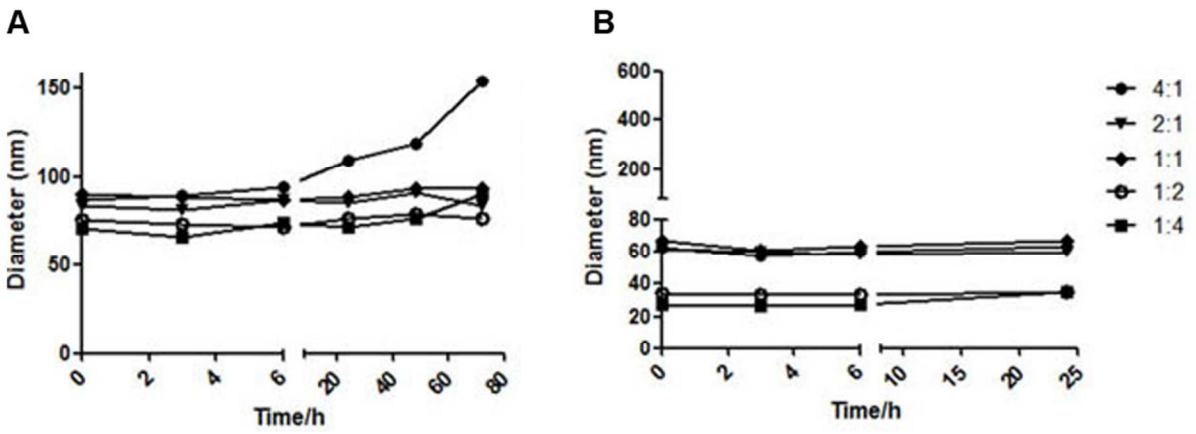


Figure S5. (A) Particle size change of CPTD NPs with different CPTD/CPTD-PEG_{5000} weight ratio incubated with PBS for 72 h. (B) Particle size change of CPTD NPs with different CPTD/CPTD-PEG_{5000} weight ratio incubated with FBS for 24 h.

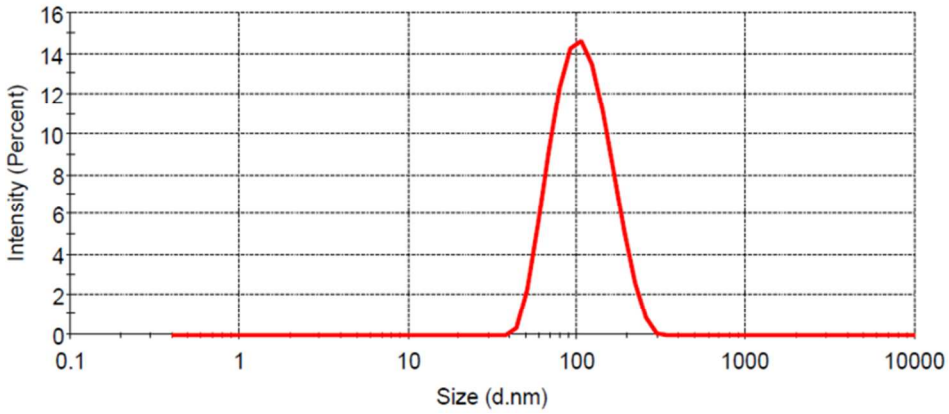


Figure S6. Particle size of CPTD NPs diluted with DI water at concentration of 0.75 μg/ml

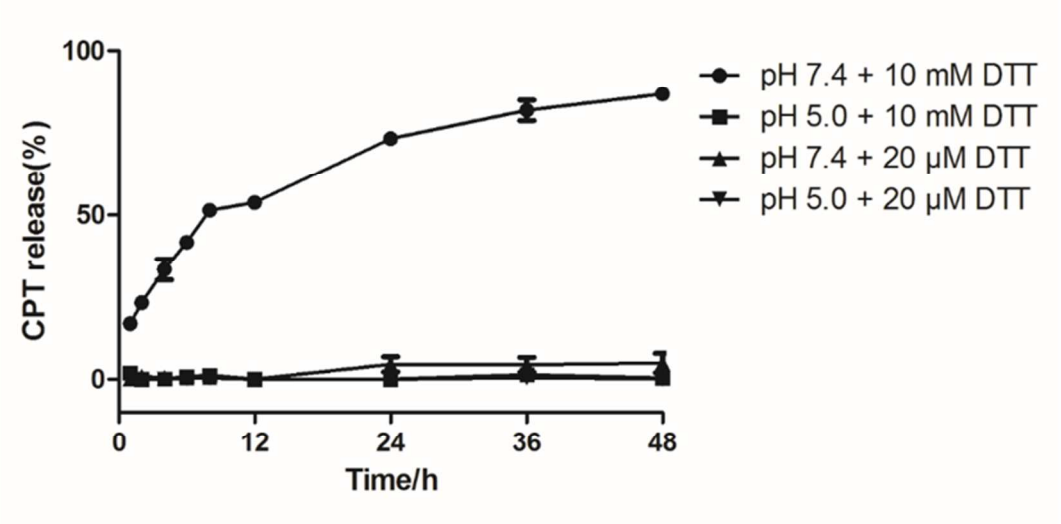


Figure S7. *In Vitro* CPT release from NT-CPTD triggered by different concentrations of DTT in PBS 7.4 or PBS 5.0 at 37 □. Data were presented as means ± SD (n = 3).

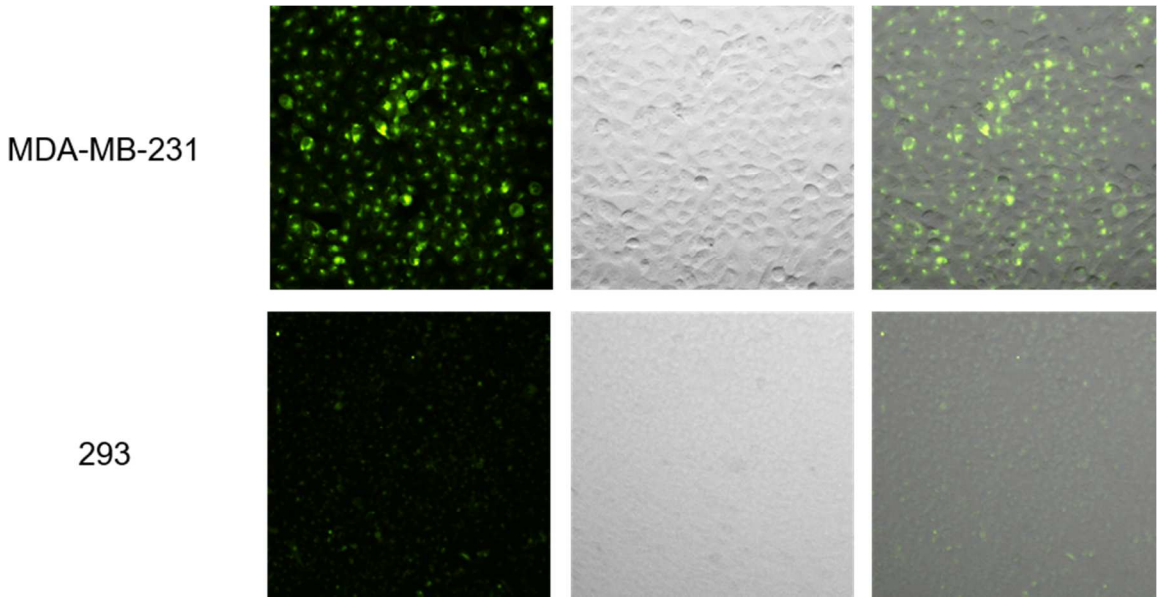


Figure S8. Cellular uptake of NT-CPTD NPs in NSTR1-positive MDA-MB-231 cells and NTSR1-negative 293 cells

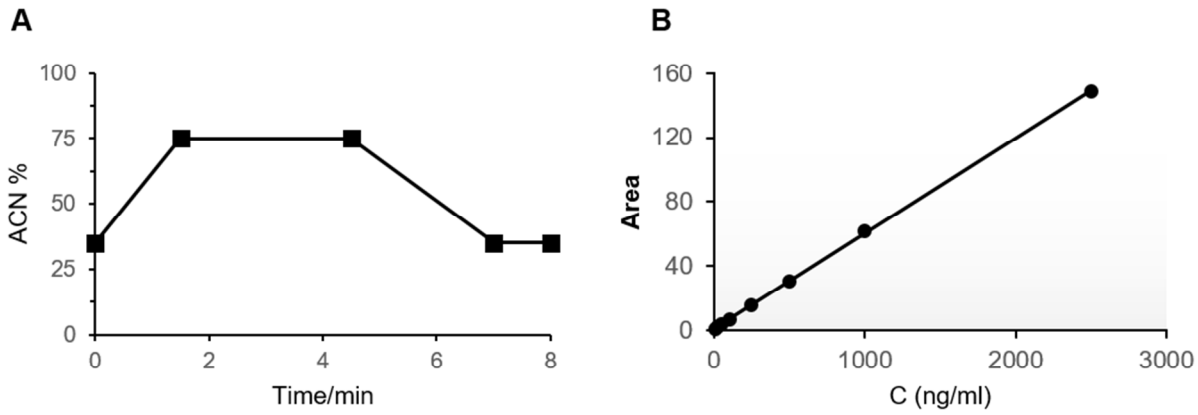


Figure S9. (A) HPLC method for CPT analysis. (B) HPLC Standard curve of CPT based on fluorescence (λ_{em}=369 nm, λ_{ex}=442 nm) (R^2=0.9997)

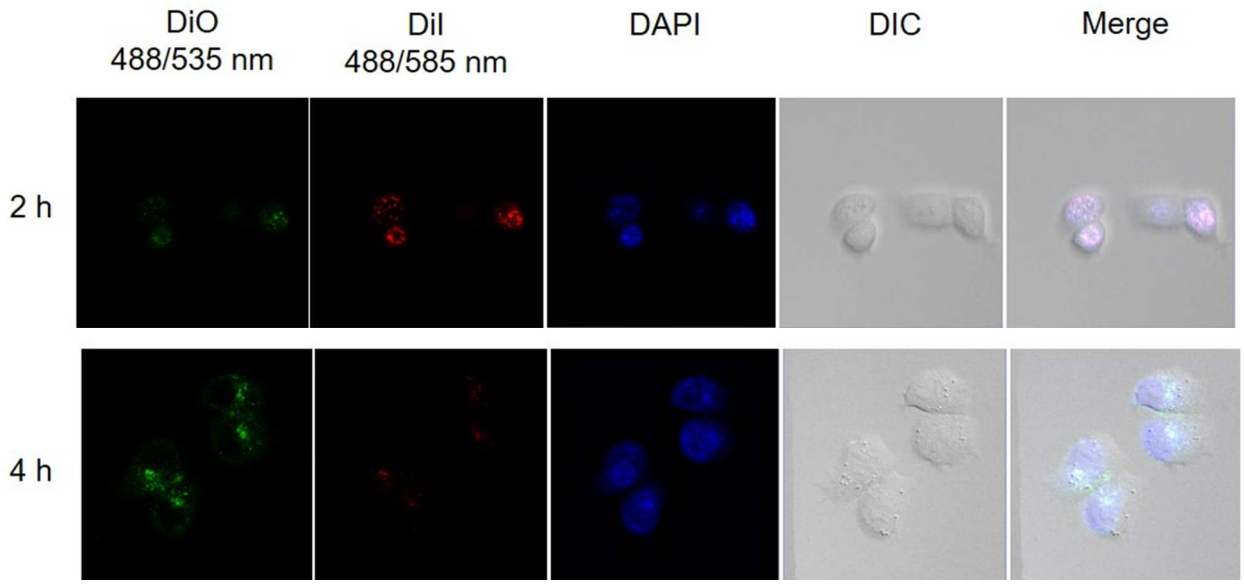


Figure S10. Confocal images of CPTD/CPTD-PEG_{5000} FRET NPs incubated in MDA-MB-231 cells for 2 h and 4 h. λ_{ex} = 488 nm, λ_{em} (DiO) = 535 ± 20 nm, λ_{em} (DiI) = 585 ± 20 nm. Fluorescence of DiI could be observed only when DiO and DiI are co- encapsulated in the NPs. All images were visualized via 63×oil immersion lens.

	PBS 7.4 Size (nm)		10 % FBS-containing buffer Size (nm)		PBS 6.5 Size (nm)	
	0 h	24 h	0 h	24 h	0 h	24 h
CPTD NPs	85.2±2.4	89.7±5.3	105.3±1.3	105.7±0.8	89.2±5.0	94.1±3.3
NT-CPTD NPs	95.7±1.7	92.1±0.5	106.0±2.8	105.2±1.8	94.0±0.8	91.8±0.5

Table S1. Size distribution of CPTD NPs and NT-CPTD NPs incubated in PBS 7.4, 10 % FBS-containing PBS 7.4 buffer and PBS 6.5 for 24 h.