Electronic Supplementary Information

Reduction-responsive disulfide linkage core-cross-linked polymeric micelles for site-specific drug delivery

Gaizhen Kuang,[a,*,#] Qingfei Zhang,[b,c,#] Shasha He,[b] Yanjuan Wu[d] and Yubin Huang[b,c,*]

[a] Department of Medical Oncology, Affiliated Cancer Hospital of Zhengzhou University, Zhengzhou 450008, P. R. China

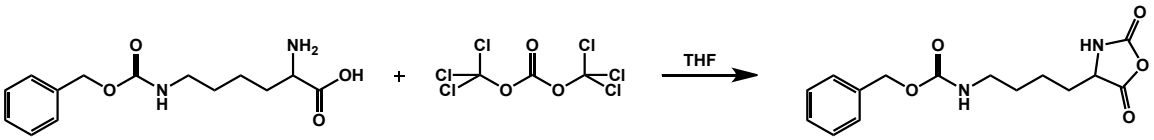
[b] State Key Laboratory of Polymer Physics and Chemistry, Changchun Institute of Applied Chemistry, Chinese Academy of Sciences, Changchun 130022, P. R. China

[c] University of Science and Technology of China, Hefei 230026, P. R. China

[d] Shandong Provincial Key Laboratory of Molecular Engineering, Qilu University of Technology-Shandong Academy of Science, Ji'nan 250353, PR China

[#] These authors contribute equally.

* Corresponding authors: gzhkuang@163.com (G. Kuang), ybhuang@ciac.ac.cn (Y. Huang)



Scheme S1. Synthesis of Lys(Z)-NCA.

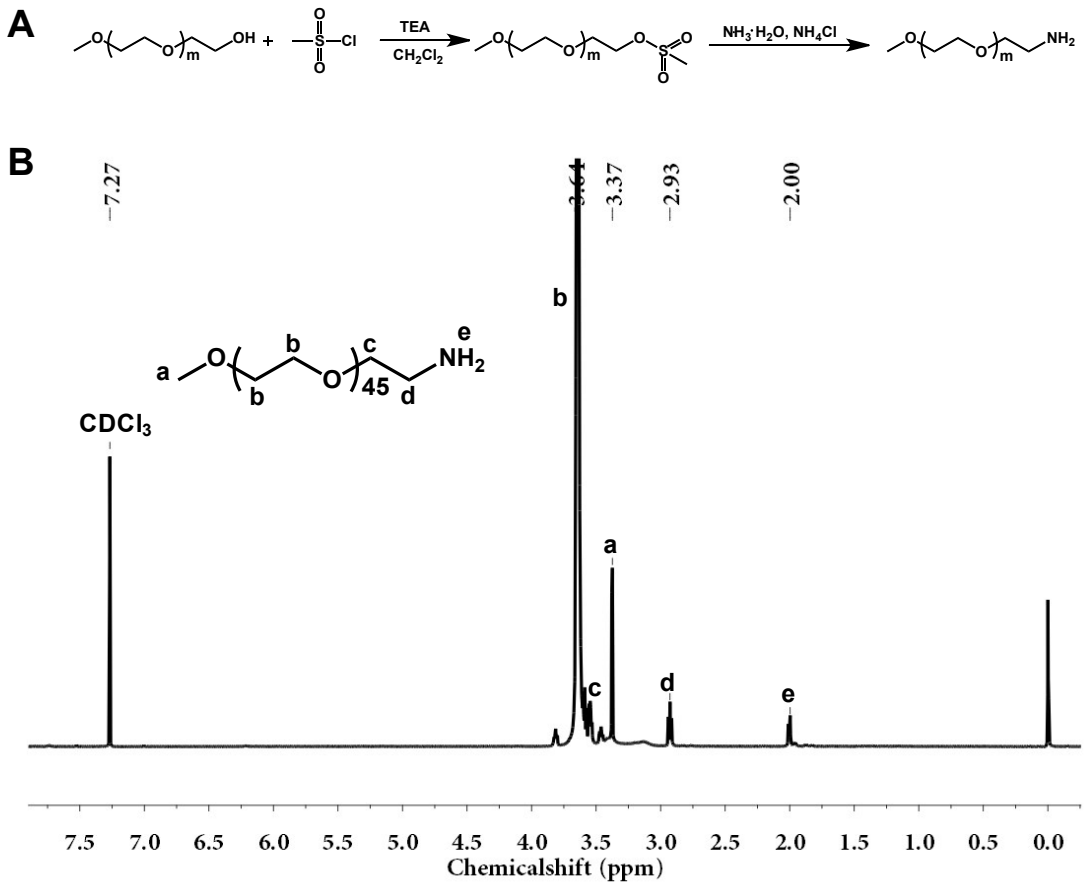


Fig. S1. Synthesis (A) and ^{1}H NMR spectrum (B) of $mPEG_{2k}$-NH_2.

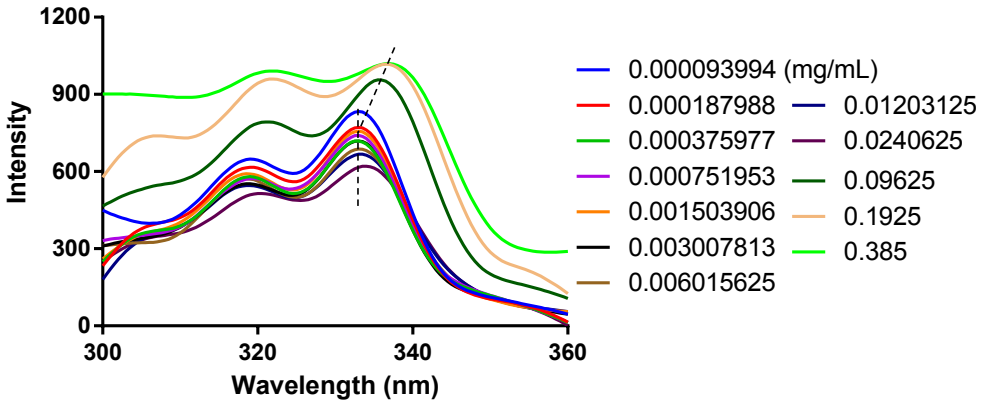


Fig. S2. Emission spectra of pyrene in aqueous solution of $mPEG_{2k}$-b-PLL/LA at different concentrations.

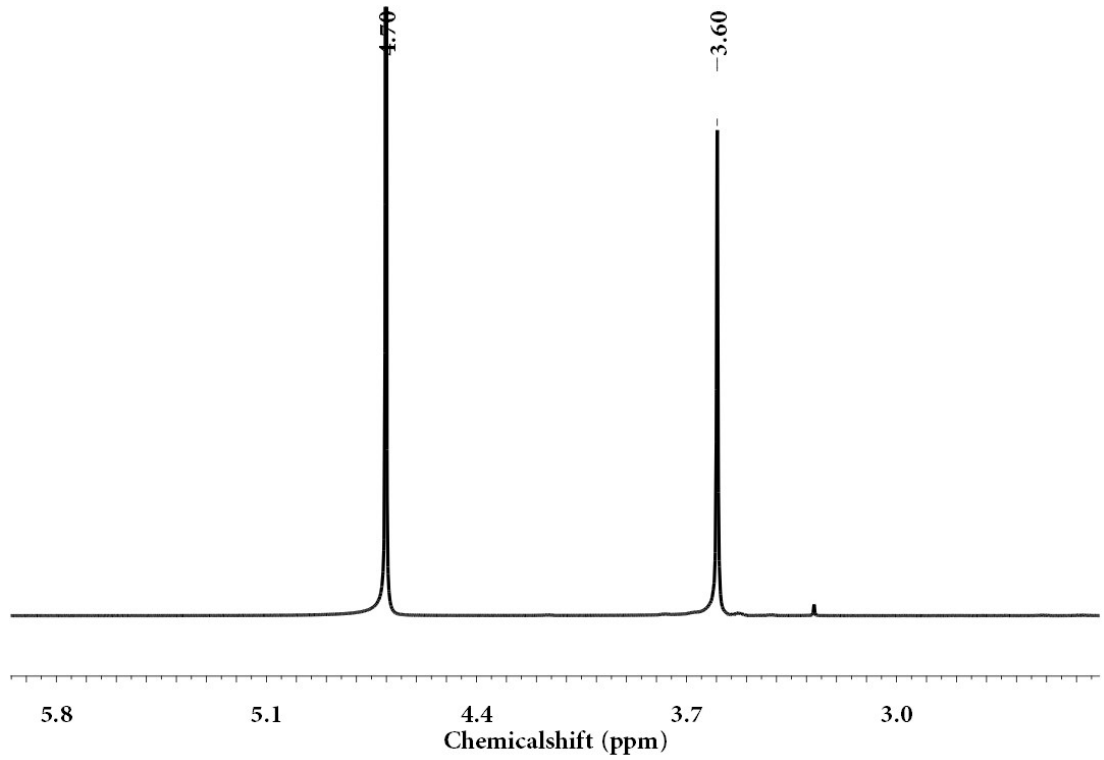


Fig. S3. ^{1}H NMR spectrum of $mPEG_{2k}$-b-PLL/LA in D_2O.

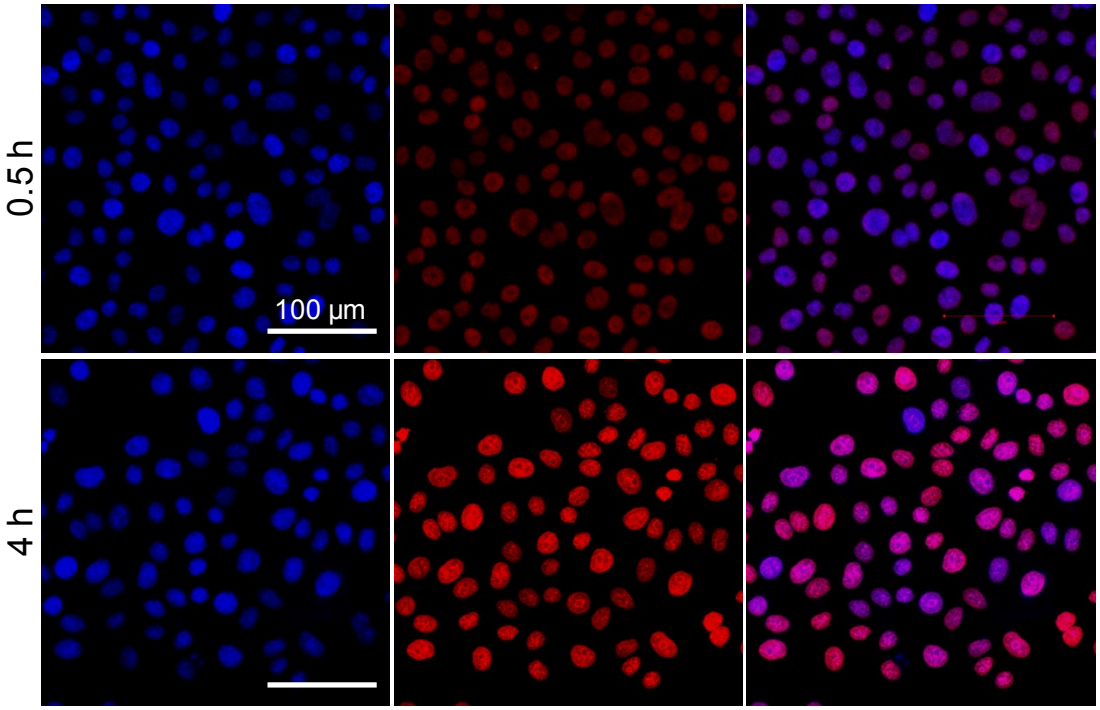


Fig. S4. Representative CLSM images of Hela cells incubated with DOX for 0.5 h or 4 h.

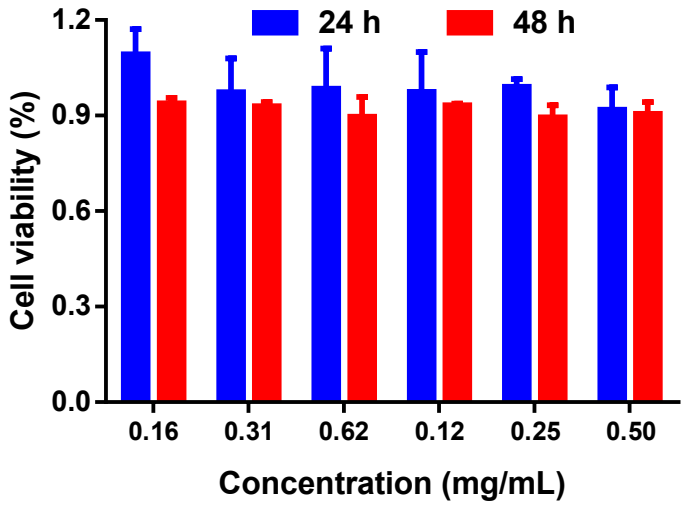


Fig. S5. Cell viability of L929 cells incubated with $mPEG_{2k}$-b-PLL/LA for different 24 h or 48 h. Three replicates for each sample were used.

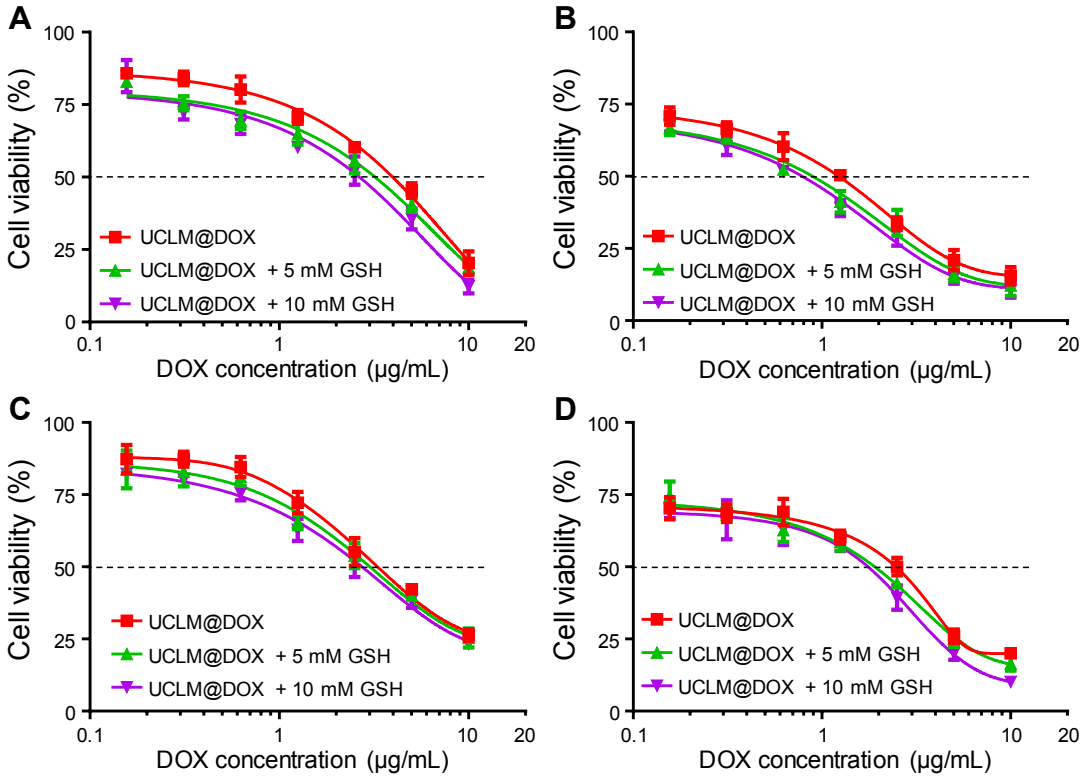


Fig. S6. Anti-cancer efficacy of UCLM@DOX. Cell viability curves of Hela cells incubated with different drugs for 24 h (A) or 48 h (B). Cell viability curves of A549 cells incubated with different drugs for 24 h (C) or 48 h (D).

Table S1. IC_{50} values of UCLM@DOX against different cells in the absence or presence of GSH.

24 h	Cell lines	CLM@DOX	CLM@DOX + 5 mM GSH	CLM@DOX + 10 mM GSH
IC_{50} (μg/mL)	Hela	3.30	2.40	1.87
	A549	3.36	2.89	2.62
48 h	Cell lines	CLM@DOX	CLM@DOX + 5 mM GSH	CLM@DOX + 10 mM GSH
IC_{50} (μg/mL)	Hela	0.93	0.66	0.59
	A549	1.56	1.31	1.08

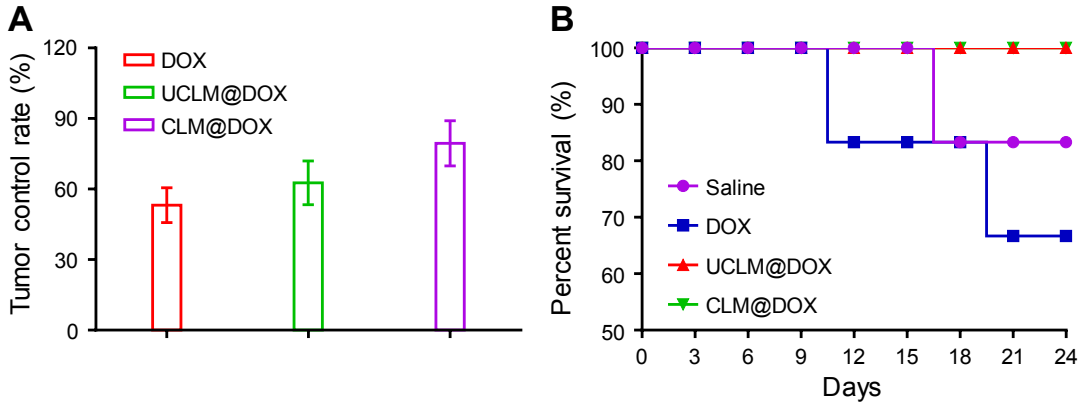


Fig. S7. (A) Tumor control rate of DOX, UCLM@DOX and CLM@DOX treatment groups at day 24. (B) Survival rate curves of mice during the experiment.

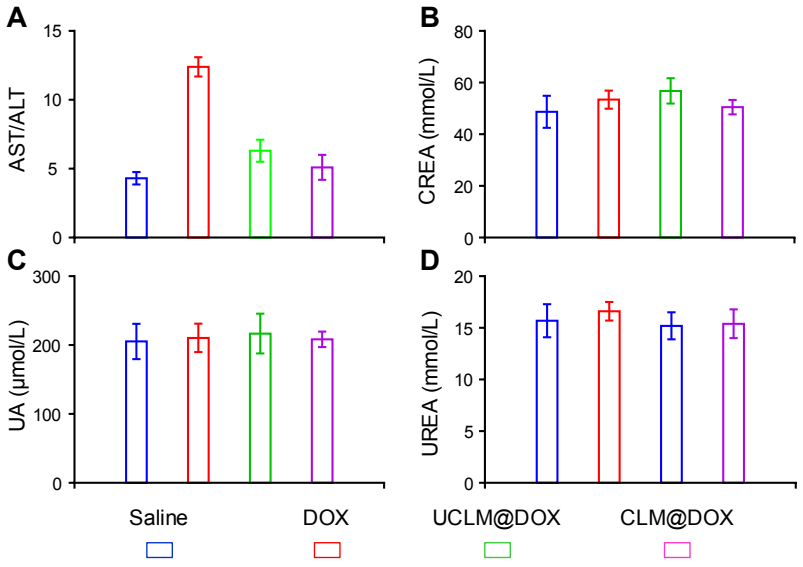


Fig. S8. Alteration of (A) AST/ALT, (B) CREA, (C) UA, (D) UREA levels of mice at the end of the treatments.

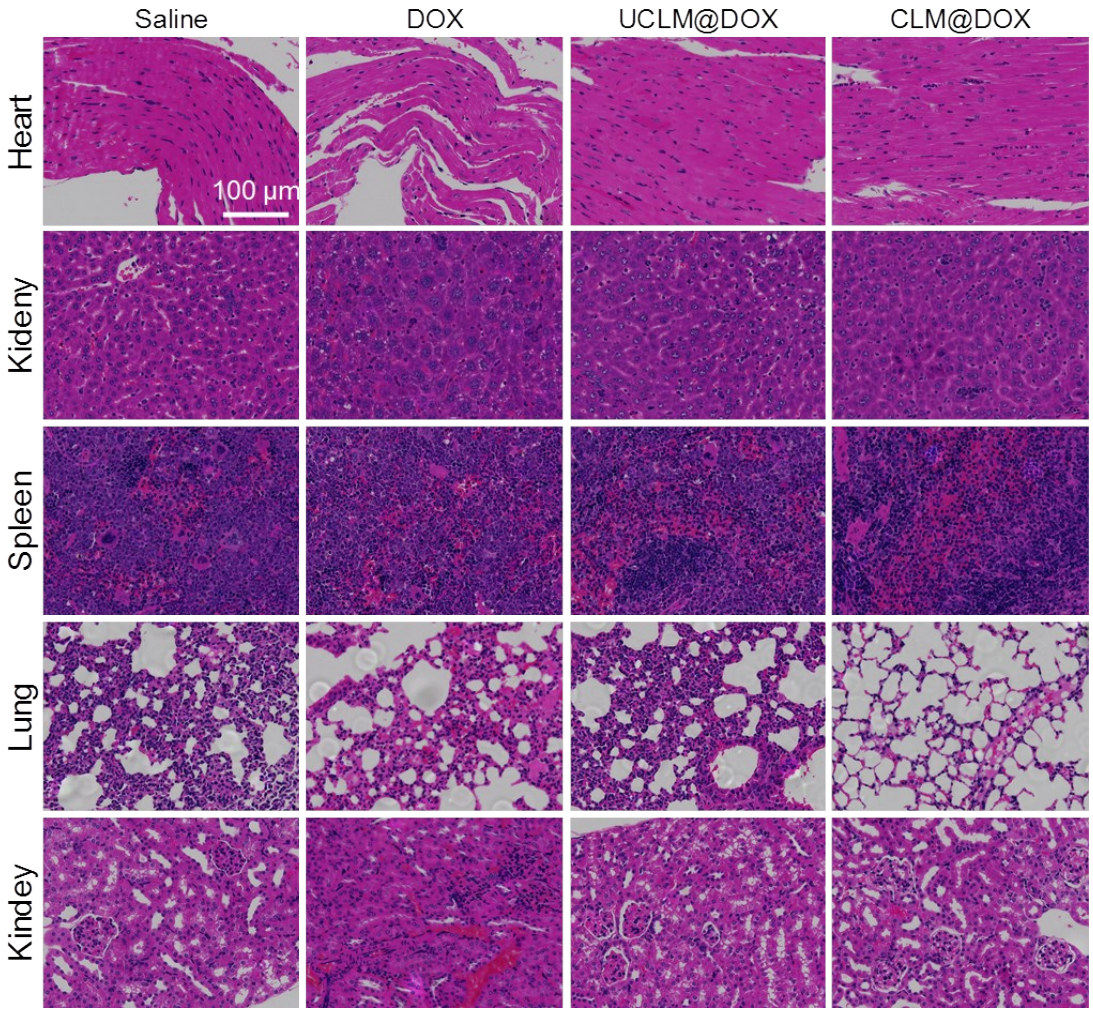


Fig. S9. H&E staining analyses of major tissues at the end of treatment.