Supporting Information

Tumor-targeting intracellular drug delivery based on dual acid/reduction-degradable nanoassemblies with ketal interface and disulfide core locations

Arman Moini Jazani, Newsha Arezi, Chaitra Shetty, Sung Hwa Hong, Haowen Li, Xiangtao Wang, Jung Kwon Oh

+ Department of Chemistry and Biochemistry, Concordia University, Montreal, Quebec, Canada H4B 1R6; § Institute of Medicinal Plant Development (IMPLAD), Chinese Academy of Medical Sciences & Peking Union Medical College, No. 151, Malianwa North Road, Haidian district, Beijing 100193, China.

Corresponding author: J.K.Oh (john.oh@concordia.ca)
Figure S1. First-order kinetic plot over time (a), evolution of molecular weight and molecular weight distribution (b), and overlaid GPC traces over conversion (c) for RAFT polymerization of HMssEt in the presence of P4 macro-RAFT agent. Conditions: [HMssEt]₀/[P4]₀/[AMBN]₀ = 50/1/0.3 in anisole at 73 °C, HMssEt/anisole = 0.6 wt/wt.

Figure S2. GPC trace of P5 diblock copolymer, compared with P4 macro-RAFT agent.
Figure S3. DLS diagram of aqueous micelles self-assembled from P5 at 1 mg/mL.

Figure S4. DLS diagrams to show colloidal stability in the presence of serum proteins.
Figure S5. $^1$H-NMR spectrum of P5 incubated with DCl in CDCl$_3$.

Figure S6. $^1$H-NMR spectra in CDCl$_3$ for precipitate (a) and supernatant (b) of degraded micelles resulted from the incubation in acidic buffer at pH= 5.4.
**Figure S7.** GPC trace of precipitate and supernatant of the degraded micellar dispersion after incubation in acidic buffer pH= 5.4, compared with P4 and P5.

![GPC trace](image)

**Figure S8.** UV/Vis spectrum of a mixture of aqueous Dox-micelles (1 mL) with DMF (5 mL).

![UV/Vis spectrum](image)
**Figure S9.** Calibration curves constructed with maximum fluorescence intensity at 593 nm over Dox concentration in buffer solutions at pH = 5.4 and pH = 7.4 with and without 10 mL GSH.

**Figure S10.** %Dox release from Dox-NPs in triplicate being incubated at pH 7.4 (control with no stimuli).
Figure S11. Fluorescence microscopy images of HeLa cells incubated with Dox-NPs (as encapsulated Dox), compared with the control (with not Dox-NPs) at pH = 7.4. Scale bar = 100 μm.
**Figure S12.** Fluorescence microscopy images of HeLa cells incubated with Dox-NPs (as encapsulated Dox), compared with the control (with not Dox-NPs) at pH = 6.8 with 10 mM GSH-OEt. Scale bar = 100 µm.