Supporting information

Self-assembled Micelles of PEG-Poly(Disulfide Carbamate Amine) Copolymers for Intracellular Dual-Responsive Drug Delivery

Chao Lin⁎, Bo Loua, Jie Zhaoa, Rong Jinb, Peng Zhaoa, Jianbo Lic, and Jie Ren⁵

a Shanghai East Hospital, The Institute for Biomedical Engineering and Nanoscience, Tongji University School of Medicine, Tongji University, Shanghai 200092, PR China.
b Institute of Nanochemistry and Nanobiology, Shanghai University, Shanghai 200444, PR China.
c Institute of Nano and Biopolymeric Materials, School of Materials Science and Engineering, Tongji University, 4800 Caoan Road, Shanghai, 201804, P.R. China.

Tel: 0086-21-65988029; Fax: 0086-21-65983706-0;
* Corresponding authors.
E-mail: chaolin@tongji.edu.cn
1. $^1$H NMR spectra of PEG-SSPUA copolymers

a) PEG-SSMDE

$^1$H NMR (D$_2$O) $\delta$ (ppm) = 4.33 (SSCH$_2$CH$_2$); 3.65 (CH$_2$CH$_2$O); 3.55 (OCONHCH$_2$); 3.38 (CH$_2$N(CH$_3$)CH$_2$); 3.00 (CH$_2$N(CH$_3$)CH$_2$); 2.95 (SSCH$_2$CH$_2$).

b) PEG-SSPDA

$^1$H NMR (D$_2$O) $\delta$ (ppm) = 4.32 (SSCH$_2$CH$_2$); 3.76 (NCH$_2$CH$_2$N); 3.65 (CH$_2$CH$_2$O); 3.57 (OCONHCH$_2$); 3.45 (OCONHCH$_2$CH$_2$); 2.97 (SSCH$_2$CH$_2$).
c) PEG-SSBAP

$^1$H NMR (D$_2$O, ppm): $\delta$ 4.30 (SSCH$_2$CH$_2$), 3.65 (CH$_2$CH$_2$O); 3.4-4.0 (NCH$_2$CH$_2$N), 3.31 (OCONHCH$_2$), 3.21 (OCONHCH$_2$CH$_3$), 2.95 (SSC$_2$H$_2$CH$_2$), 1.95 (CH$_2$CH$_2$CH$_2$CH$_2$).

Figure S1. $^1$H NMR spectra analysis of PEG-SSPCA copolymers. a) PEG-SSMDE; b) PEG-SSPDA; c) PEG-SSBAP.

Figure S2. FT-IR spectrum of PEG-SSBAP copolymers showing characteristic peak of carbamate linkage.
3. GPC of PEG-SSPCA copolymers

Figure S3. GPC curve of PEG-SSPCA copolymers. a) PEG-SSMDE; b) PEG-SSPDA; c) PEG-SSBAP.
Figure S4. a) Acid-base titration curve of PEG-PCA copolymers; b) Acid-base titration of PEG-SSBAP copolymer gives pH value as the function of apparent protonation degree of tertiary amines in PEG-SSBAP copolymer.
Figure S5. The ratio of fluorescence intensity at 372 and 383 nm (from pyrene excitation spectra) as a function of the concentrations of PEG-SSBAP.

Figure S6. CLSM observation of intracellular distribution of Dox 1 h after incubating free Dox (up) or Dox-loaded PEG-SSBAP micelles (down) with SKOV-3 cells.
Figure S7. CLSM observation of intracellular location of Dox 4 h after incubating Dox-loaded PEG-SSBAP micelles with MCF-7 cells. This figure indicates Dox-loaded micelles (in red) locate in the lysosomes (in green) stained by LysoTracker green DND26 (Lyso). The cellular nucleus in blue is stained by DAPI. The arrow shows the co-localization of Dox-loaded micelles and lysosome.
Figure S8. Cytotoxicity of BAP and cysteamine, as degradation products from PEG-SSBAP, at varied concentration from 5 to 400 μg·mL\(^{-1}\) against three types of cell lines: a) MCF-7, b) HepG2 and c) SKOV-3 cells. PBS group was used as a blank control and set as 100% cell viability.
**Figure S9.** TUNEL (a) and Ki67 (b) staining of tumor section of the mice 28 day after chemotherapy using Dox-loaded PEG-SSBAP micelles. PBS group was used as a positive control.

**Figure S10.** H&E staining of other organ section of the mice 28 day after chemotherapy using Dox-loaded PEG-SSBAP micelles. PBS group was used as a control.