Supporting Information

Synthesis, self-assembly and drug release behaviors of reduction-labile multi-

responsive block miktobrush quaterpolymers with linear and V-shaped grafts

Wentao Wu, Wenxue Dai, Xiaoqi Zhao, Jian Zhang and Youliang Zhao*

Suzhou Key Laboratory of Macromolecular Design and Precision Synthesis, Jiangsu Key Laboratory of Advanced Functional Polymer Design and Application, State and Local Joint Engineering Laboratory for Novel Functional Polymeric Materials, College of Chemistry, Chemical Engineering and Materials Science, Soochow University, Suzhou 215123, China



Scheme S1 Synthetic routes to 3-hydroxy-2-maleimidylpropyl 2-bromo-2-methylpropanoate (HMBP).

sample	$M_{\rm n,NMR}$ (kDa)	$f_{\mathrm{w,PEG}}$ (%)	$f_{\mathrm{w,PNIPAM}}$ (%)	$f_{\mathrm{w,PAA}}$ (%)	<i>f</i> _h (pH 7.4)	<i>f</i> _h (pH 5.3)
B4a	68.2	13.2	27.6	26.9	0.676	0.618
B4b	87.3	10.3	21.6	42.9	0.747	0.654
B4c	108	8.33	17.4	53.6	0.792	0.675

Table S1. Influence of solution pH on hydrophilic fraction (f_h) of B4a-B4c copolymers at 25 °C



Fig. S1 1 H (a) and 13 C (b) NMR spectra of HMBP recorded in CDCl₃.



Fig. S2 FT-IR spectrum of HMBP.



Fig. S3 ¹H NMR spectrum of PSH recorded in CDCl₃.



Fig. S4 FT-IR spectra of various disulfide-functionalized copolymers.



Fig. S5 ¹H NMR spectra of B3b (a) and B3c (b) recorded in CDCl₃.



Fig. S6 ¹H NMR spectra of B3a (a) and B4a (b) recorded in DMSO- d_6 .



Fig. S7 Influence of chain length of PAA grafts on transmittances of copolymer aggregates formed from B4a-B4c copolymers in aqueous solution ($c_p = 1.0 \text{ mg mL}^{-1}$).



Fig. S8 Influence of pH and reduction stimuli on DLS plots of B4b (a-d) and B4c (e-h) aggregates $(c_p = 0.50 \text{ mg mL}^{-1})$ formed in PBS solution at 25 °C.



Fig. S9 TEM images of copolymer aggregates ($c_p = 0.50 \text{ mg mL}^{-1}$) formed from B4b (a-d) and B4c (e-h) in PBS solution at 25 °C with or without pH/redox stimuli: (a, e) pH 7.4; (b, f) pH 5.3; (c, g) pH 7.4 + 10 mM DTT; (d, h) pH 5.3 + 10 mM DTT.



Fig. S10 DLS plots of blank and DOX-loaded B4a aggregates ($c_p = 0.50 \text{ mg mL}^{-1}$) formed in PBS solution (pH 7.4, 50 mM) at 37 °C.



Fig. S11 TEM image of DOX-loaded B4a aggregates ($c_p = 0.50 \text{ mg mL}^{-1}$) formed in PBS solution (pH 7.4, 50 mM) at 37 °C.



Fig. S12 Relative fluorescence intensities from blank B4a aggregates, DOX-loaded B4a aggregates and free DOX internalized by 4T1 cells at a DOX dose of 10 μ g mL⁻¹ after 2- or 6-h incubation using flow cytometry.