Supplementary material

Synthesis of 3-((2-(Methacryloyloxy)ethyl)thio)propanoic Acid (BSMA)

Synthesis of tert-Butyl-3-((2-Hydroxyethyl)thio)propanoate. *tert*-Butyl acrylate (10.0 g, 78 mmol) and TEA (9.47 g, 93.6 mmol) were dissolved in anhydrous CH_2Cl_2 (50 mL) and cooled to 0 ^oC in an ice-water bath. 2-Mercaptoethanol (6.1 g, 78 mmol) in anhydrous CH_2Cl_2 (20 mL) was added dropwise over 30 min. Then the reaction mixture was stirred at ambient temperature overnight. The mixture was washed with saturated NH_4Cl (3 x 100 mL) and NaCl solution, sequentially. The organic layer was collected and dried over anhydrous Na_2SO_4. After filtration, the filtrate was evaporated to dryness on a rotary evaporator. After drying in a vacuum oven overnight a colorless oil was obtained (14.2g, yield: 88.2%). ^1H NMR ($CDCl_3$, δ, ppm, TMS; Figure S1a): 3.70-3.77 (2H, HOCH_2CH$_2$-), 2.70-2.79 (4H, -SCH_2CH_2OCO-), 2.50-2.55 (2H, HOCH$_2$CH_2S-), 2.18 (1H, *H*O-), and 1.46 (9H, -OCO(CH_3)$_3$).

Synthesis of 2-((3-(tert-Butoxy)-3-Oxopropyl)thio)ethyl Methacrylate. TEA (2.83 g, 28 mmol) and *tert*-butyl-3-((2-hydroxyethyl)thio)propanoate (5.0 g, 24 mmol) were dissolved in anhydrous CH_2Cl_2 (40 mL) and cooled to 0 ^oC in an ice-water bath. Methacryloyl chloride (2.63 g, 25 mmol) in anhydrous CH_2Cl_2 (15 mL) was then added dropwise over 30 min. The reaction mixture was stirred at 0 ^oC for 2 h and then overnight at room temperature. The mixture was filtered off, washed with saturated $NaHCO_3$ and further purified by neutral alumina column chromatography using CH_2Cl_2 as the eluent. After drying in a vacuum oven overnight a colorless oil was obtained (5.75 g, yield: 75.4%). ^1H NMR ($CDCl_3$, δ, ppm, TMS; Figure S1b): 5.57-6.11 (2H, CH_2=C(CH$_3$)-), 4.30 (2H, -OCH_2CH$_2$-), 2.80 (4H, -SCH_2CH_2OCO-), 2.53 (2H, -C(=O)OCH$_2$CH_2S-), 1.94 (3H, CH$_2$=C(CH_3)-), and 1.46 (9H, -OCO(CH_3)$_3$).

Synthesis of 3-((2-(Methacryloyloxy)ethyl)thio)propanoic Acid (BSMA). 2-((3-(*tert*-Butoxy)-3-oxopropyl)thio)ethyl methacrylate (3.0 g, 11 mmol) was dissolved in anhydrous CH_2Cl_2 (5 mL). Then TFA (5 mL) was added. The reaction mixture was stirred at room temperature for 5 h and the mixture was evaporated to dryness on a rotary evaporator to afford BSMA (1.95 g, yield: 65%). ^1H NMR ($CDCl_3$, δ, ppm, TMS, Figure S1c): 5.57-6.11 (2H, CH_2=C(CH$_3$)-), 4.30 (2H, -OCH_2CH$_2$-), 2.81-2.90 (4H, -SCH_2CH_2OCO-), 2.70 (2H, -C(=O)OCH$_2$CH_2S-), and 1.94 (3H, CH$_2$=C(CH_3)-).

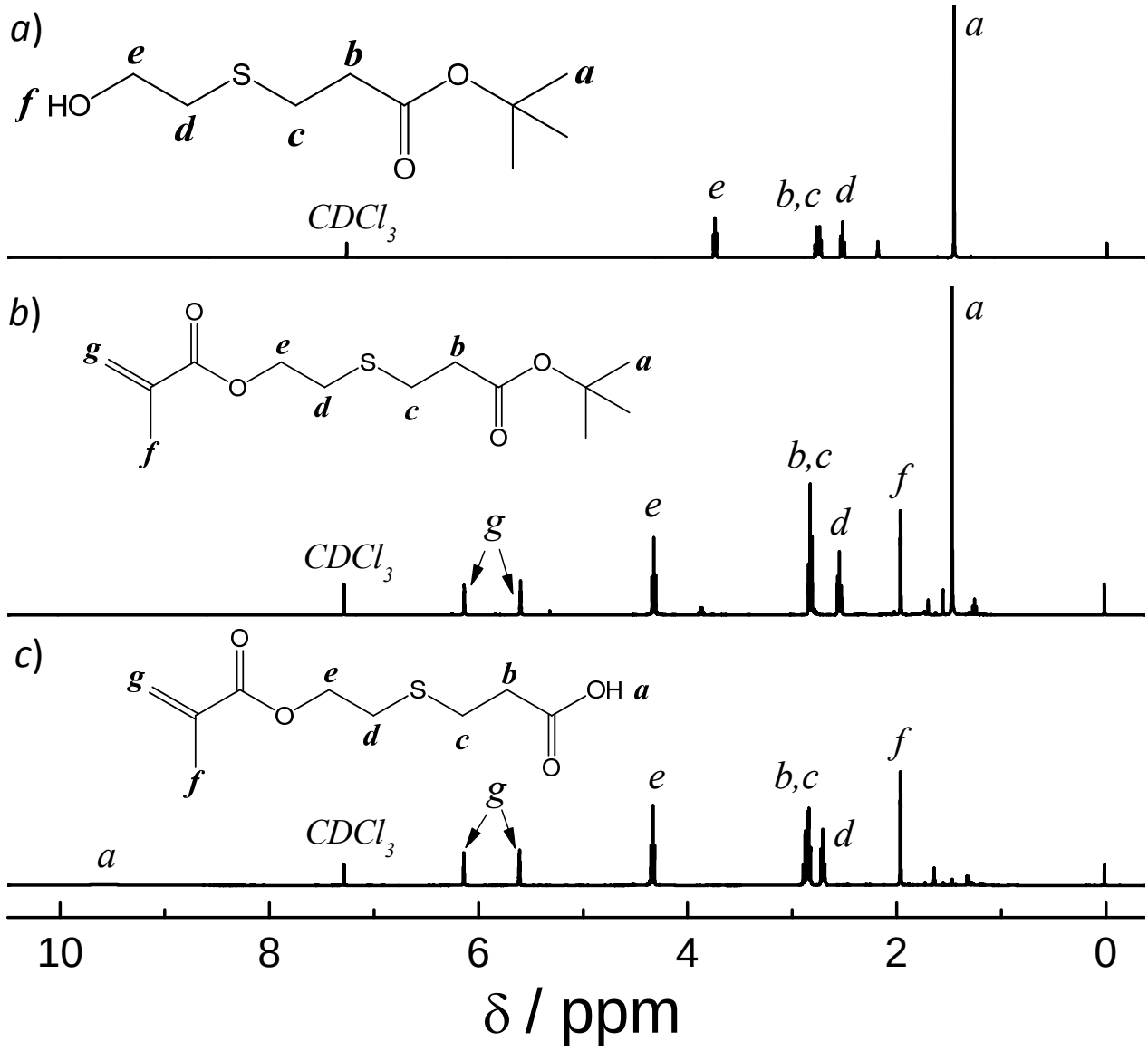

Figure S1. ^{1}H NMR spectra recorded in $CDCl_3$ for (a) *tert*-butyl-3-((2-hydroxyethyl)thio)propanoate, (b) 2-((3-(*tert*-butoxy)-3-oxopropyl)thio)ethyl methacrylate, and (c) 3-((2-(methacryloyloxy)ethyl) thio)propanoic acid (BSMA).

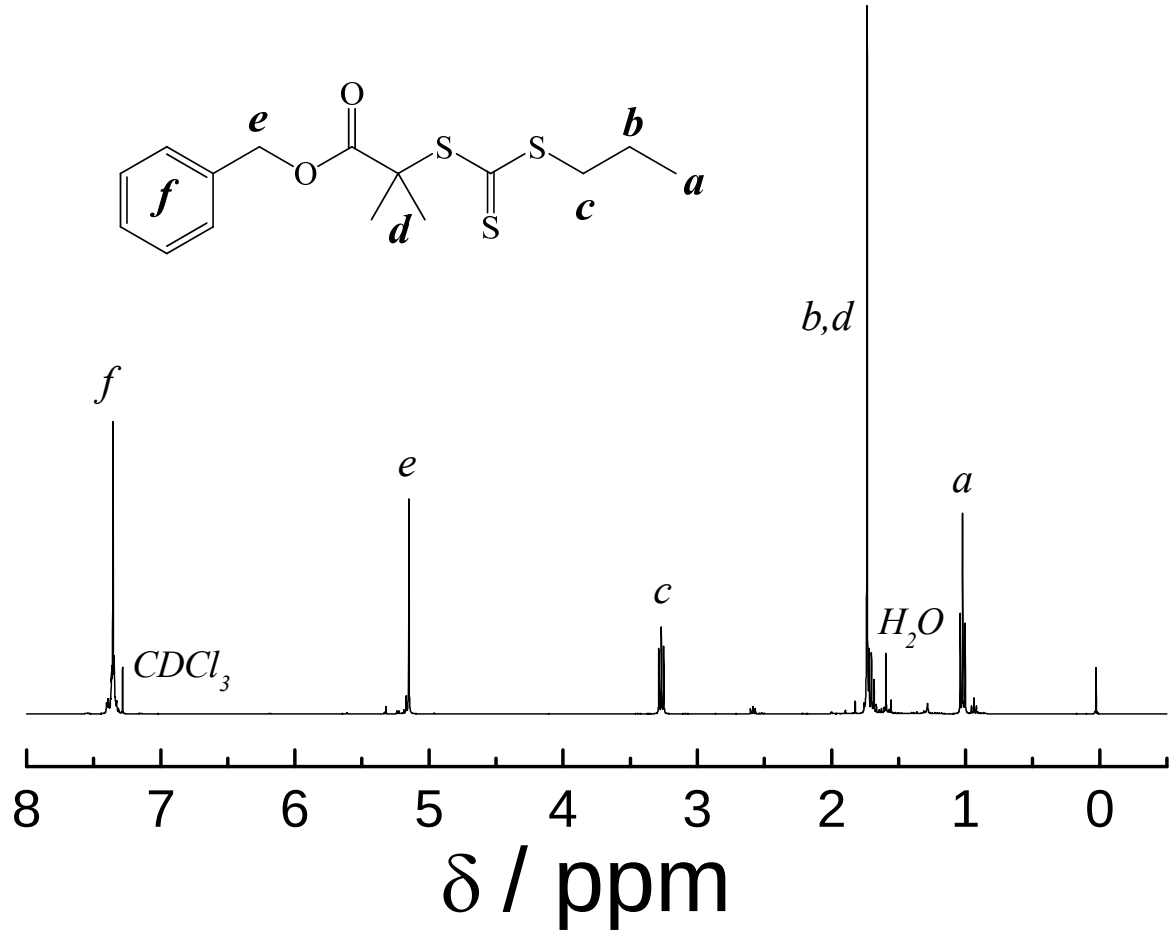

Figure S2. ^{1}H NMR spectrum recorded for BPTPA in $CDCl_3$.

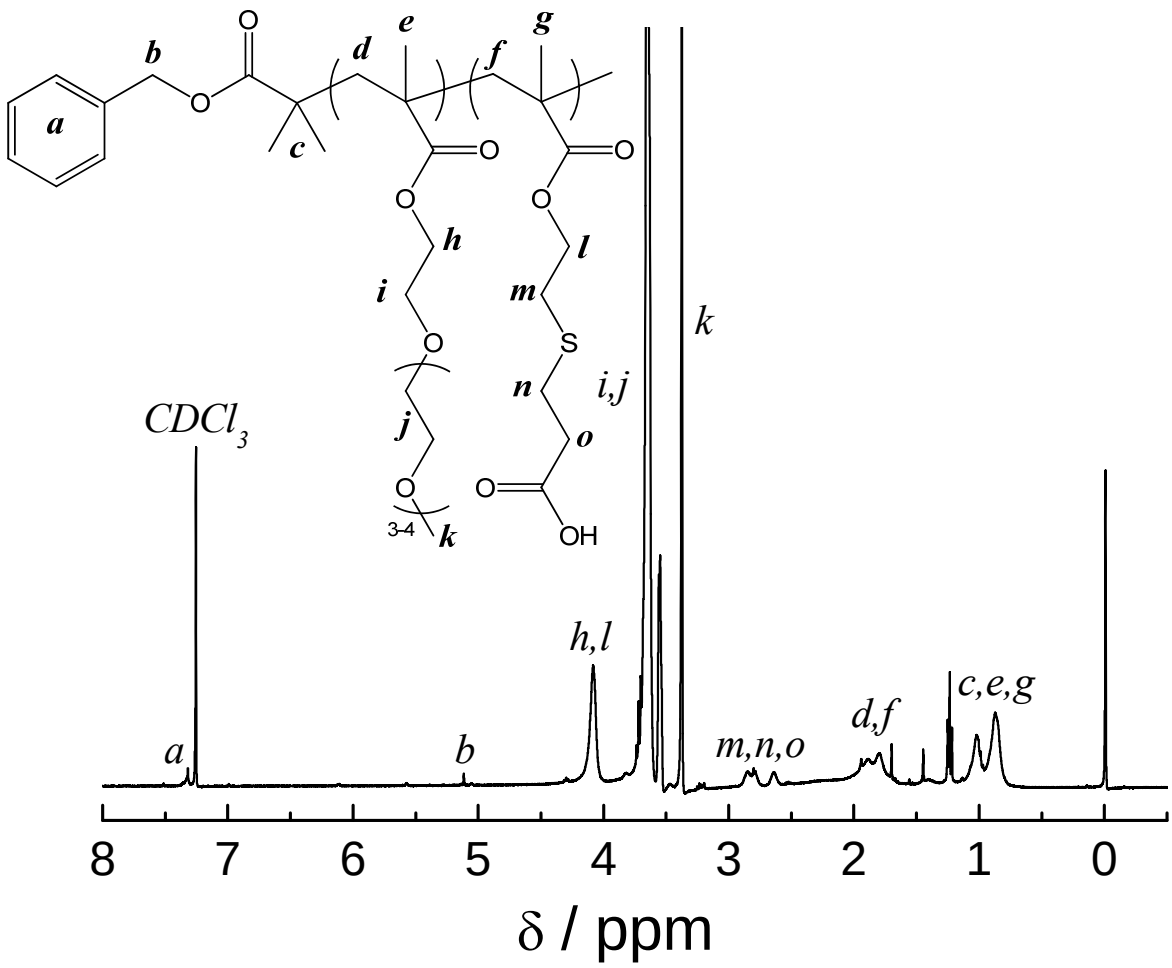

Figure S3. ^{1}H NMR spectrum recorded for P(OEGMA-*co*-BSMA) in $CDCl_3$.

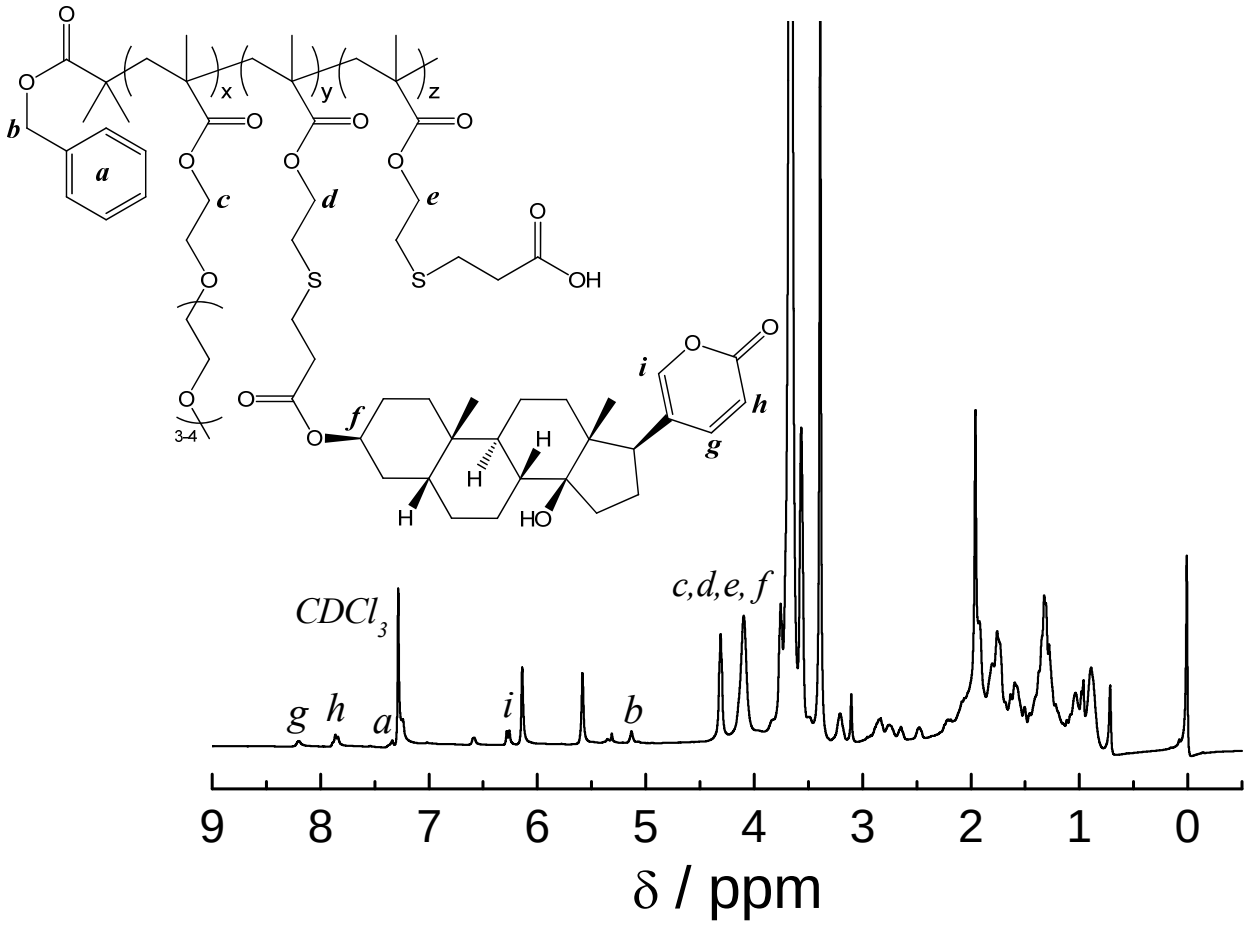

Figure S4. ^{1}H NMR spectrum recorded for P(OEGMA-*co*-BUF-*co*-BSMA) in $CDCl_3$.

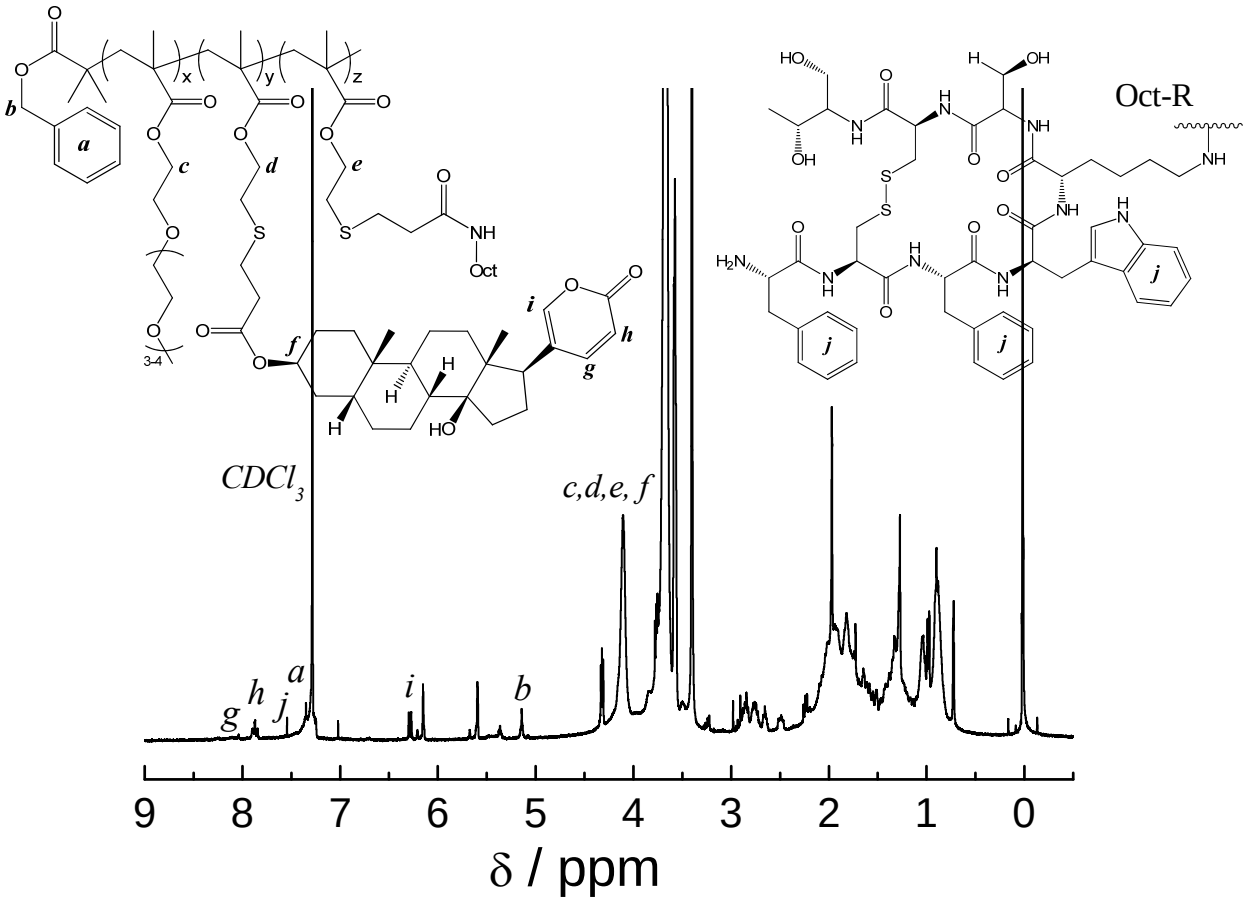

Figure S5. ^{1}H NMR spectrum recorded for P(OEGMA-*co*-BUF-*co*-Oct) in $CDCl_3$.

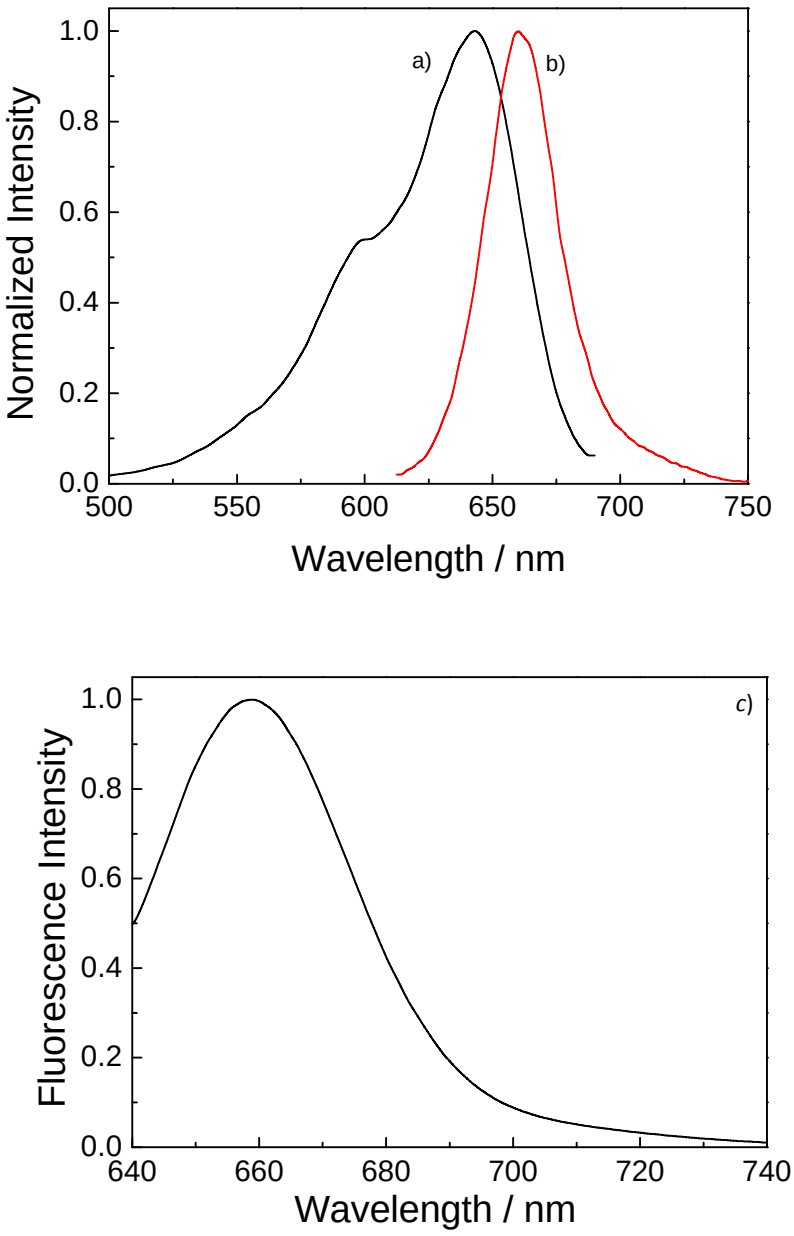

Figure S6. Fluorescence (a) excitation and (b) emission spectra recorded for P(OEGMA-*co*-BUF-*co*-Oct-*co*-Cy5) (0.1 g/L, [Cy5] = 3.0 x 10^{-6} M; slit widths: ex. 5 nm, em. 5 nm). (c) Fluorescence emission spectrum recorded for P(OEGMA-*co*-BUF-*co*-Cy5) (0.1 g/L, [Cy5] = 3.0 x 10^{-6} M; λ_{ex} = 633 nm, slit widths: ex. 5 nm, em. 5 nm).

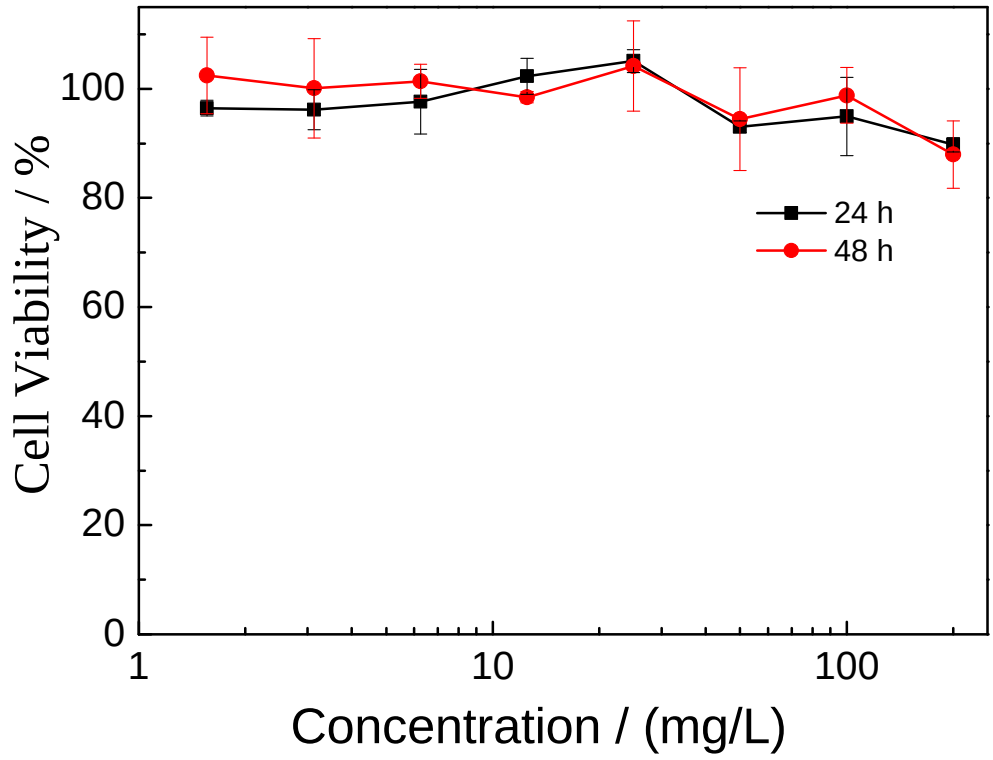

Figure S7. Viability of MCF-7 cells after incubation for 24 h and 48 h in the presence of P(OEGMA-*co*-Oct) at varying concentrations.

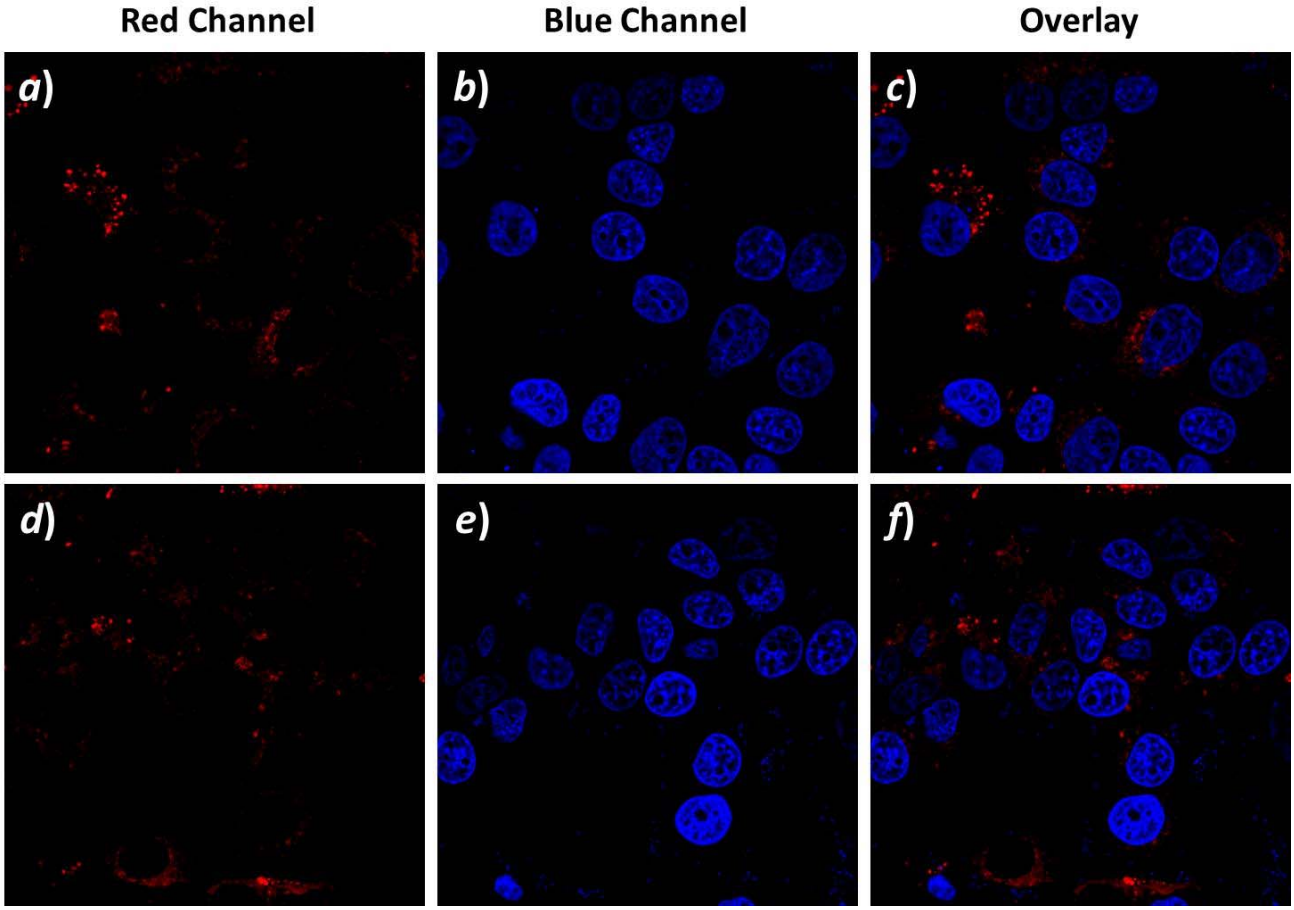

Figure S8. Typical confocal microscopy fluorescence images recorded for MDA-MB-231 cells after incubating at 37 ºC with (top panel) P(OEGMA-*co*-BUF-*co*-Oct-*co*-Cy5) ([Cy5] = 3.0 x 10^{-6} M) and (bottom panel) P(OEGMA-*co*-BUF-*co*-Cy5) ([Cy5] = 3.0 x 10^{-6} M) for 4 h. (a and d) The red channel was excited at 633 nm and collected between 660-700 nm. (b and e) The cell nuclei were stained by DAPI and the blue channel was excited at 405 nm and collected between 420-460 nm. (c and f) Overlay of the blue and red channels.

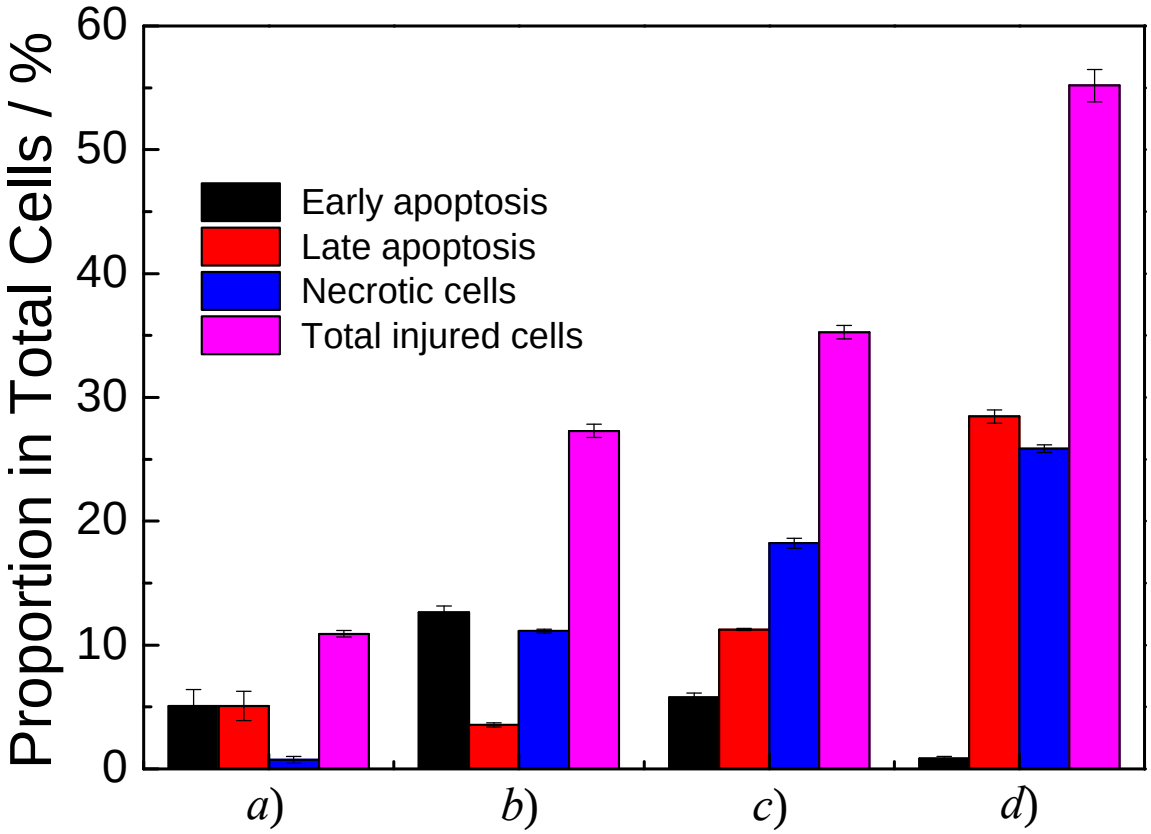

Figure S9. The proportion of early apoptosis, late apoptosis, and necrotic cells (a) untreated and treated with 50 nM BUF-equivalent dosage of (b) free BUF, (c) P(OEGMA-*co*-BUF), and (d) P(OEGMA-*co*-BUF-*co*-Oct) for 24 h were quantitatively summarized. Annexin-v FITC/PI double staining assay was employed to detect the apoptosis of cells.

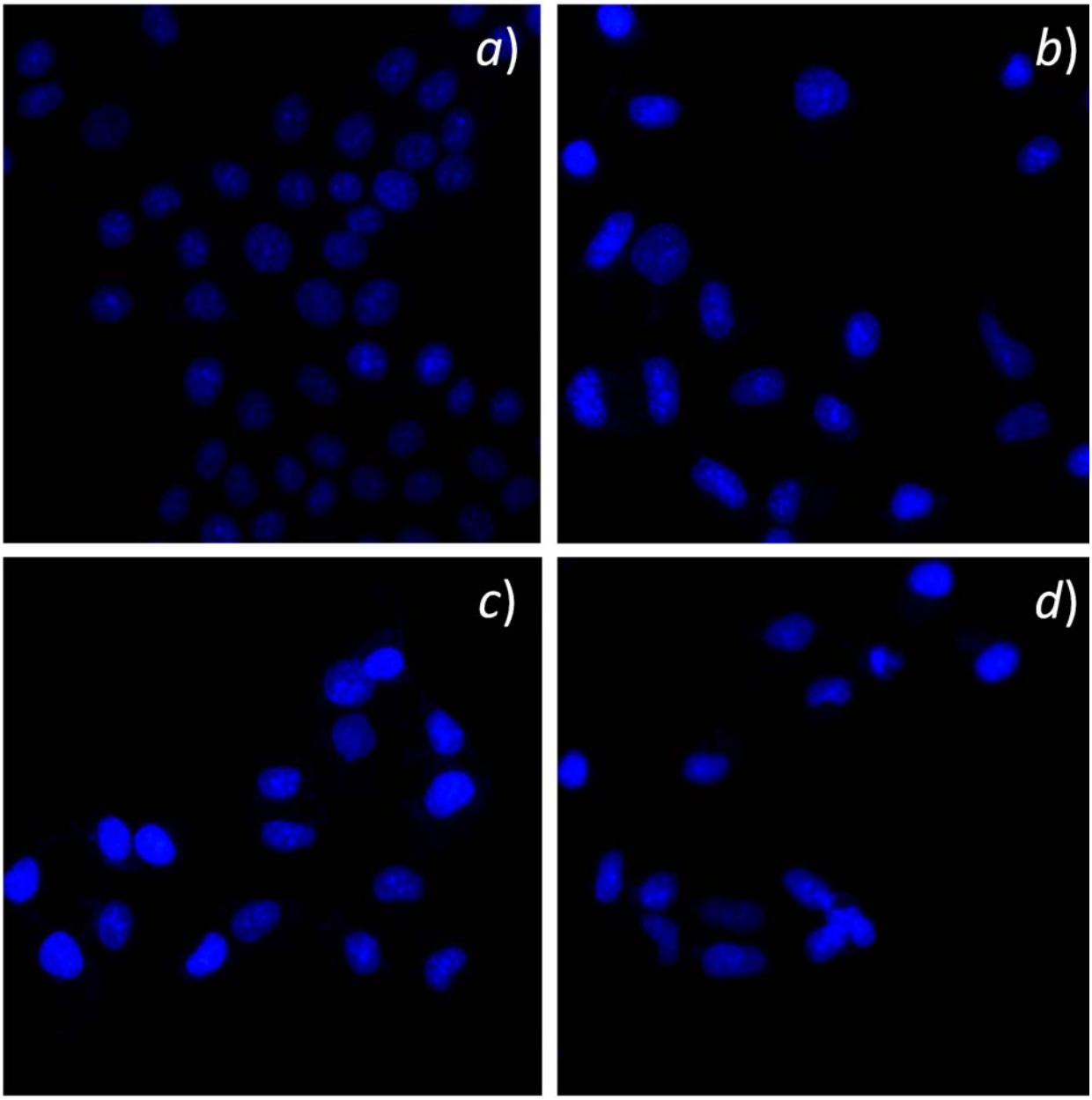

Figure S10. BUF-containing polymeric micelles induced apoptosis of MCF-7 cells as detected by DAPI nuclear staining (excitation: 405 nm; blue channel: 440-480 nm). Typical CLSM images of MCF-7 cells after incubation for 24 h in the (a) absence and presence of 50 nM BUF-equivalent dosage of (b) free BUF, (c) P(OEGMA-*co*-BUF), and (d) P(OEGMA-*co*-BUF-*co*-Oct).

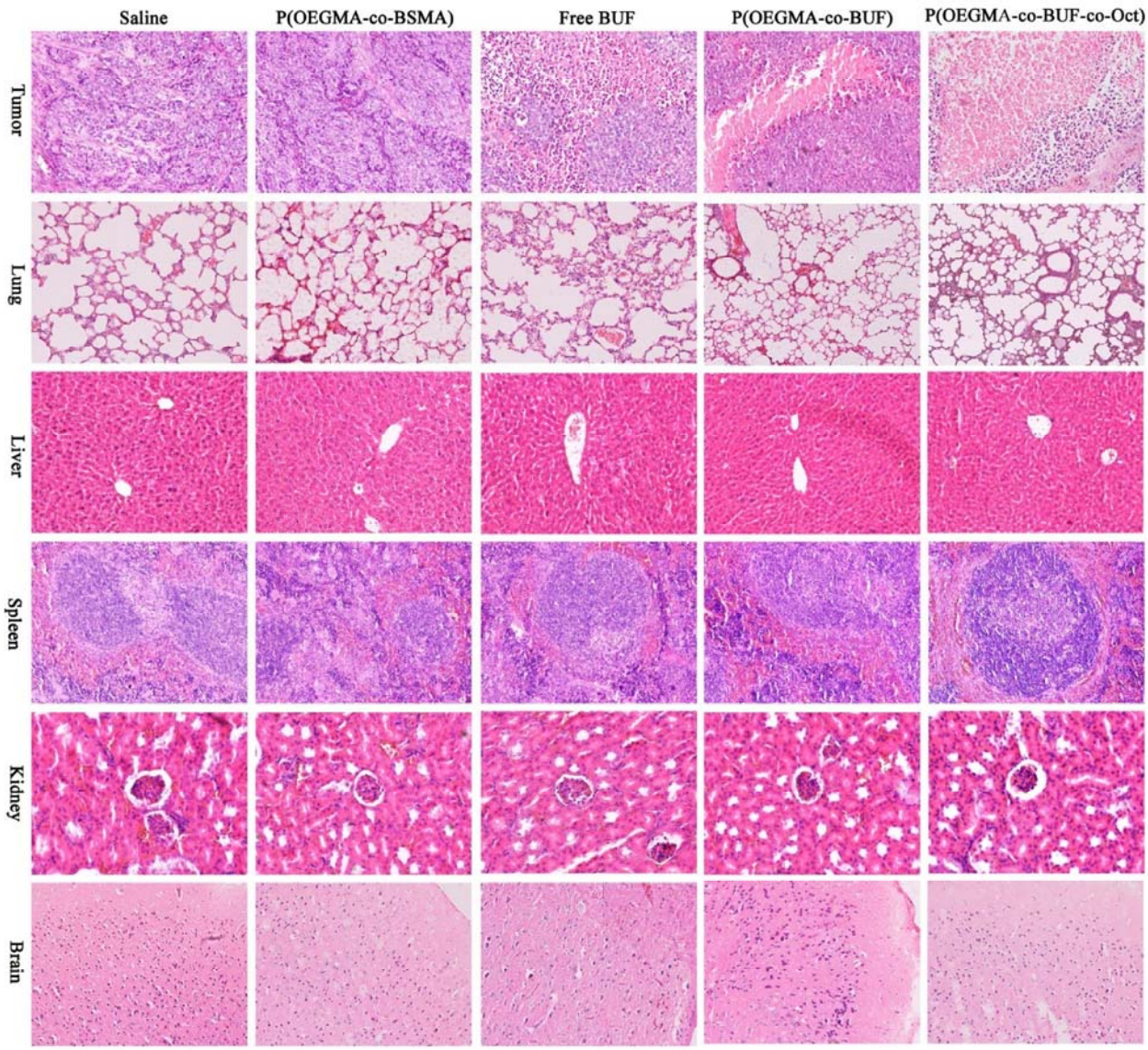

Figure S11. HE staining of tumor tissues after receiving the treatment of saline, P(OEGMA-*co*-BSMA), BUF, P(OEGMA-*co*-BUF), and P(OEGMA-*co*-BUF-*co*-Oct).