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Supporting Information

Combining the Power of Heat and Light: Temperature-Programmed Photoinitiated RAFT Dispersion Polymerization To Tune Polymerization-Induced Self-Assembly

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Materials:

2-Hydroxypropyl methacrylate (HPMA, Aladdin), monomethoxy poly(ethylene glycol) ($mPEG_{113}$, 5000 g/mol, Sigma-Aldrich), glycidyl methacrylate (GlyMA, Aladdin), dicyclohexylcarbodiimide (DCC, Aladdin), 4-dimethylaminopyridine (DMAP, Aladdin), sodium 2, 2-dimethyl-2-silapentane-5-sulfonate (DSS, Aladdin) hydroquinone (Aladdin), *N*,*N*-dimethylformamide (DMF, Tianjin Damao) were used as received. 4-Cyano-4-(ethylthiocarbonothioylthio) pentanoic acid (CEPA) was synthesized according to a published procedure[1]. Sodium phenyl-2,4,6-trimethylbenzoylphosphinate (SPTP) was synthesized according to a literature procedure[2]. LED lamps (405 nm) were purchased from Huaenopto (Zhejiang).

Characterization

Transmission Electron Microscopy (TEM). The obtained dispersions were diluted 100-fold with water. A drop of the solution was placed on a copper grid for 1 min and then blotted with filter paper to remove excess solution. A drop of uranyl acetate solution (0.5 wt%) was soaked on the same copper grip for 1.5 min, and then blotted with filter paper to remove excess strain. Transmission electron microscopy (TEM) observations were carried out on a Hitachi 7700 instrument operated at 120 kV.

Scanning electron microcopy (SEM). SEM images were collected using a Hitachi S4800 electron microscope on samples sputter-coated with gold prior imaging. The samples for SEM imaging were prepared by drop casting the diluted dispersion on mica films and drying at ambient temperature prior to sputter-coating.

Gel Permeation Chromatography (GPC). The molecular weight and polydispersity of the block copolymers were measured by gel permeation chromatography (GPC) at 60 ºC using a Waters 1515 GPC instrument with dimethylformamide (DMF) as the mobile phase using Waters styragel HR1 and HR4 columns. The eluent used was HPLC grade DMF containing 10 mM LiBr and was filtered prior to use. The flow rate of DMF was 1.0 mL/min. Linear poly(methyl methacrylate) polymers with narrow molecular weight distributions were used as the standards to calibrate apparatus.

^{1}H NMR Spectroscopy. Nuclear magnetic resonance (NMR) spectra were recorded in D_2O or DMSO using a Bruker Avance III HD 400 MHz NMR spectrometer at a temperature of 25 °C.

UV-visible absorption spectroscopy. Optical transmittance of the polymeric micelles at various temperatures (heating rate was 0.5 ^{o}C/min) was measured by a UV–vis spectrophotometer (UV2450) at 500 nm.

Dynamic Light Scattering. Intensity-average hydrodynamic diameters of the dispersions (0.1% v/v) were obtained using a Brookhaven nanoparticle size-zeta potential analyzer.

Cryogenic transmission electron (Cryo-TEM). Cryo-TEM images were obtained under 200 kV by a Tecnai G2 F20.

Synthesis of mPEG$_{113}$-CEPA

A solution of CEPA (2.76 g, 10.5 mmol) in anhydrous CH_2Cl_2 (90 mL) was introduced in a dry flask under nitrogen atmosphere containing mPEG$_{113}$ (35.0 g, 7 mmol). Then a solution of DCC (2.17 g, 10.5 mmol) and DMAP (0.128 g, 1.05 mmol) in anhydrous CH_2Cl_2 (20 mL) was added dropwise to the reaction mixture at 0 °C. The esterification reaction proceeded with stirring at room temperature for 48 h. The polymer was collected by precipitation of the reaction mixture in cold diethyl ether. The product was then further purified by a flash chromatography (95:5, chloroform/methanol), and finally dried at 45 ^{o}C under vacuum to obtain a yellow powder.

^{1}H NMR (400 MHz, $CDCl_3$), 4.25 (m, 2H, -$CO_2C\mathbf{H}_2$-), 3.80-3.47 (m, -$C\mathbf{H}_2O$-), 3.37 (s, 3H, -$OC\mathbf{H}_3$), 3.34 (q, 2H, $CH_3C\mathbf{H}_2$-), 2.66 (m, 2H, -$C\mathbf{H}_2CO_2$-), 2.52 (m, 1H, $C(CN)C\mathbf{H}_2$-), 2.38 (m, 1H, $C(CN)C\mathbf{H}_2$-), 1.87 (s, 3H, $C\mathbf{H}_3C(CN)$)), 1.35 (t, 3H, $C\mathbf{H}_3CH_2$-).

Synthesis of PPEGMA$_{15}$-CTA, PGMA$_{42}$-CTA and P(GMA$_{34}$-*co*-MEO$_2$MA)-CTA

The synthesis of these macro-CTAs was followed our previous research.[3,4]

Temperature-programmed aqueous photo-PISA

In a typical experiment for the synthesis of mPEG$_{113}$-PHPMA$_{400}$ diblock copolymer nano-objects (20% w/w HPMA) at 47 ^{o}C: HPMA (2.0 g, 13.9 mmol),

$mPEG_{113}$-CEPA (0.182 g, 0.0346 mmol), and SPTP (3.6 mg, 0.0116 mmol) were weighed into a 25 mL round bottom flask. DMF (0.02 g, 0.28 mmol) was added to the reaction mixture as an internal standard. The concentration of DMF in the system is as low as 0.2% w/w, which should have no effect on the photo-PISA process. Then a certain amount of water (8.0 g in this case) was added to the flask. The reaction mixture was then purged with nitrogen for 20 min, sealed, and then irradiated by a visible light LED lamp (405 nm, light intensity of 0.5 mW/cm^2) at 47 ^oC for 1 h. The polymerization was quenched by exposure to air and the addition of a small amount of hydroquinone.

Kinetics of temperature-programmed aqueous photo-PISA

In a typical experiment for the kinetic study of temperature-programmed aqueous photo-PISA of HPMA (20% w/w HPMA, target DP of 400) at 47 ^oC: HPMA (2.0 g, 13.9 mmol), $mPEG_{113}$-CEPA (0.182 g, 0.0346 mmol), sodium 2,2-dimethyl-2-silapentane-5-sulfonate (0.06 g, 0.275 mmol), and SPTP (3.6 mg, 0.0116 mmol) were weighed into a 25 mL round bottom flask. DSS (0.06 g, 0.27 mmol) was added to the reaction mixture as an internal standard. Then a certain amount of water (8.0 g in this case) was added into the flask. The reaction mixture was then purged with nitrogen for 20 min, sealed, and then irradiated by a visible light LED lamp (405 nm, light intensity of 0.5 mW/cm^2) at 47 ^oC. Samples were withdrawn at predetermined time intervals by syringes under nitrogen, and the reaction was quenched by exposure to air and the addition of a small amount of hydroquinone. The samples were then analyzed by ^{1}H NMR spectroscopy immediately.

Synthesis of $mPEG_{113}$-P($HPMA_{320}$-*co*-$GlyMA_{80}$) by temperature-programmed aqueous photo-PISA

HPMA (1.75 g, 12.2 mmol), GlyMA (0.429 g, 3.016 mmol), $mPEG_{113}$-CDPA (0.2 g, 0.0381 mmol), SPTP (0.0039 g, 0.0126 mmol), and water (8.77 g) were added into a 25 mL round-bottom flask. DMF (0.02 g, 0.28 mmol) was added to the reaction mixture as an internal standard. The concentration of DMF in the solution is as low as 0.2% w/w, which should have no effect on the photo-PISA process. The reaction mixture was purged with nitrogen for 20 min, sealed, and then irradiated with a visible light LED lamp (405 nm, light intensity 0.5 mW/cm^2) at 47 °C for 1 h to ensure full monomer conversion.

Additional results

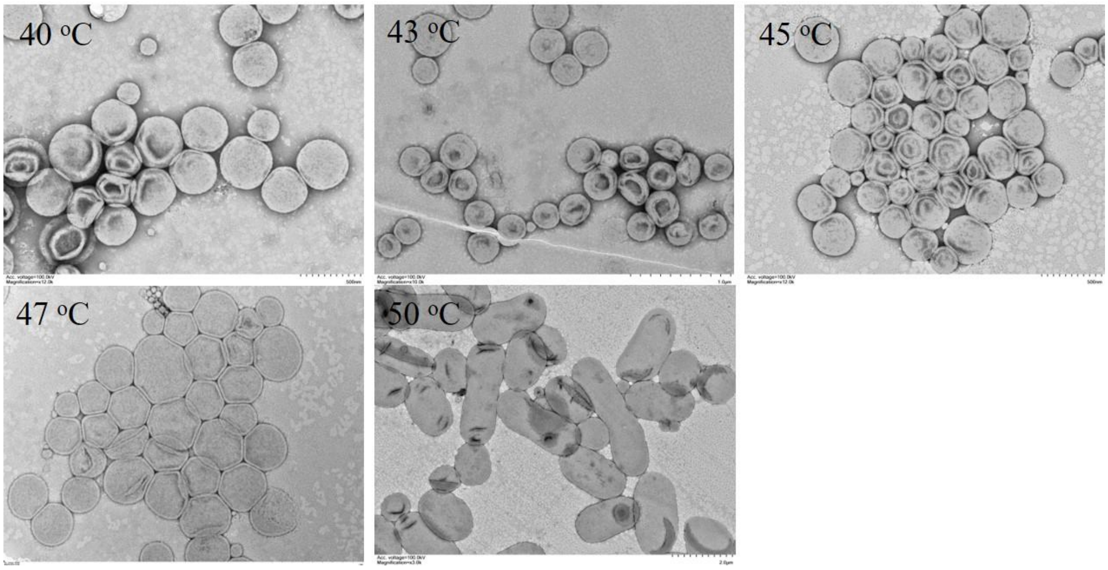

Figure S1. TEM images of mPEG$_{113}$-PHPMA$_{400}$ diblock copolymer nano-objects prepared by aqueous photo-PISA of HPMA (10% w/w HPMA concentration) using mPEG$_{113}$-CEPA as the macro-RAFT agent at different temperatures.

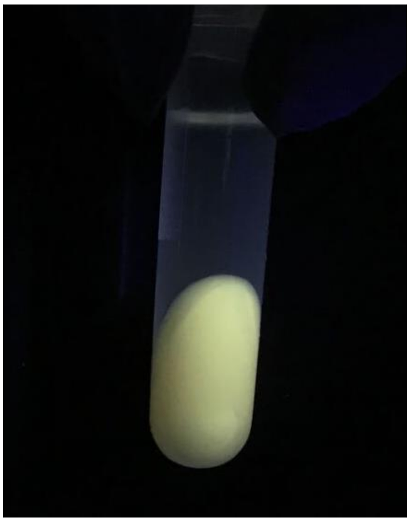

Figure S2. Photograph (under 365 nm irradiation) of centrifuge tube containing sedimented mPEG$_{113}$-PHPMA$_{400}$ LCVs (prepared at 47 ^{o}C) loaded with ecosin Y.

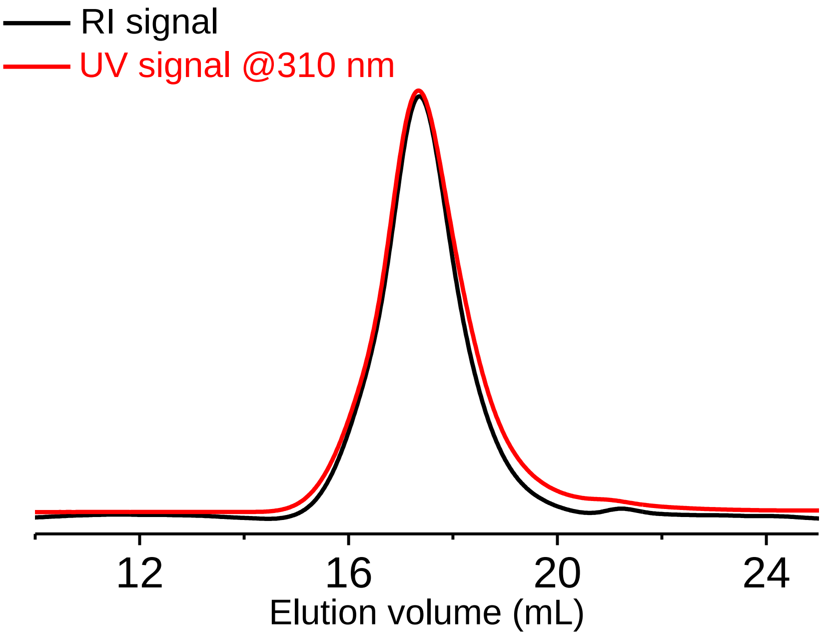

Figure S3. RI and UV (@310 nm) GPC traces of mPEG$_{113}$-PHPMA$_{400}$ diblock copolymer nano-objects prepared by aqueous photo-PISA of HPMA (10% w/w HPMA concentration) using mPEG$_{113}$-CEPA as the macro-RAFT agent at 50 °C.

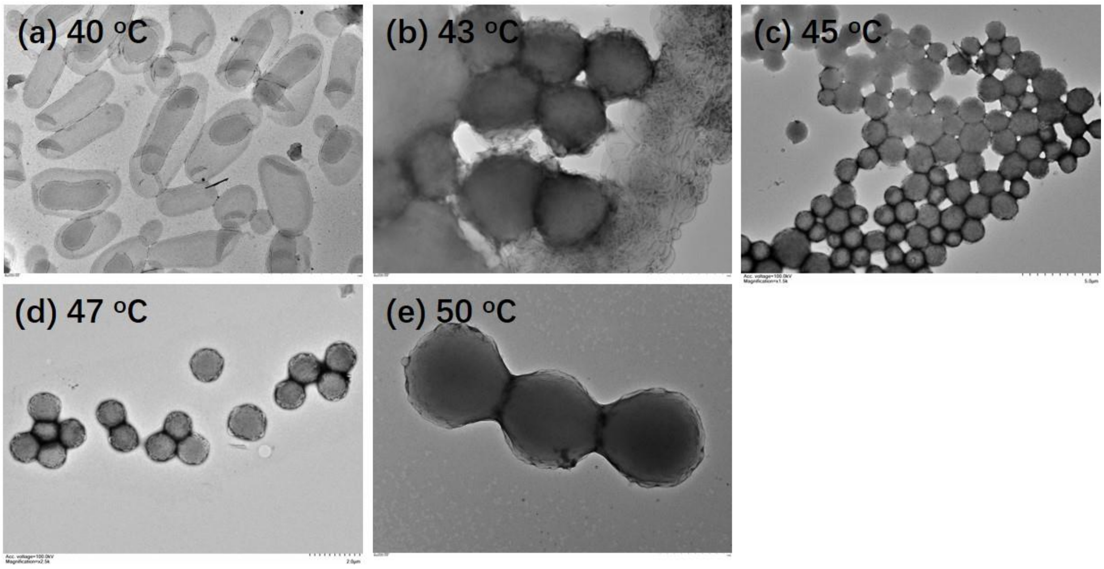

Figure S4. TEM images of mPEG$_{113}$-PHPMA$_{400}$ diblock copolymer nano-objects prepared by aqueous photo-PISA of HPMA (20% w/w HPMA concentration) using mPEG$_{113}$-CEPA as the macro-RAFT agent at different temperatures.

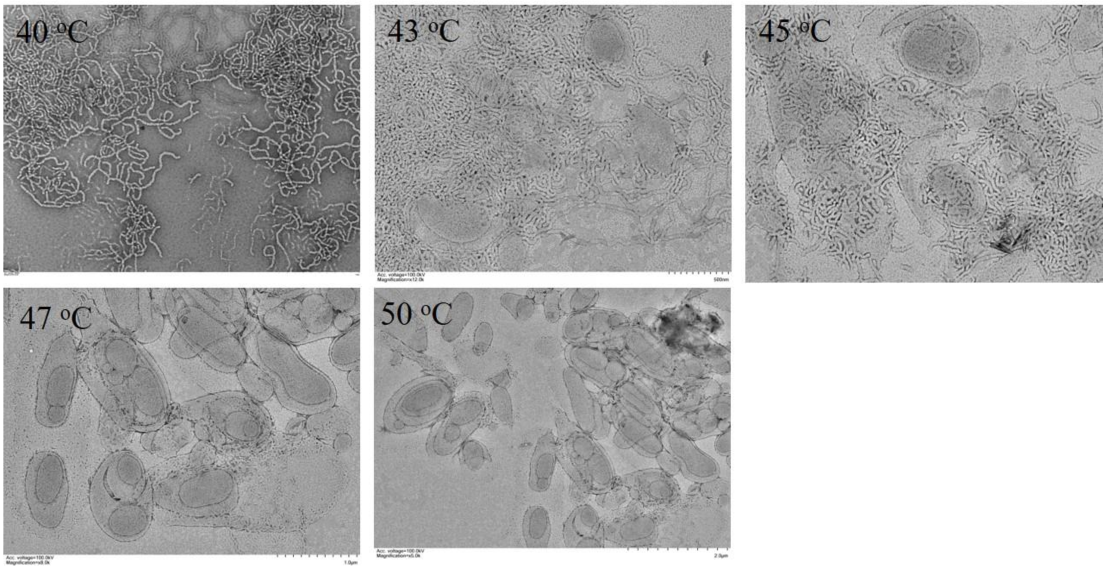

Figure S5. TEM images of mPEG$_{113}$-PHPMA$_{200}$ diblock copolymer nano-objects prepared by aqueous photo-PISA of HPMA (20% w/w HPMA concentration) using mPEG$_{113}$-CEPA as the macro-RAFT agent at different temperatures.

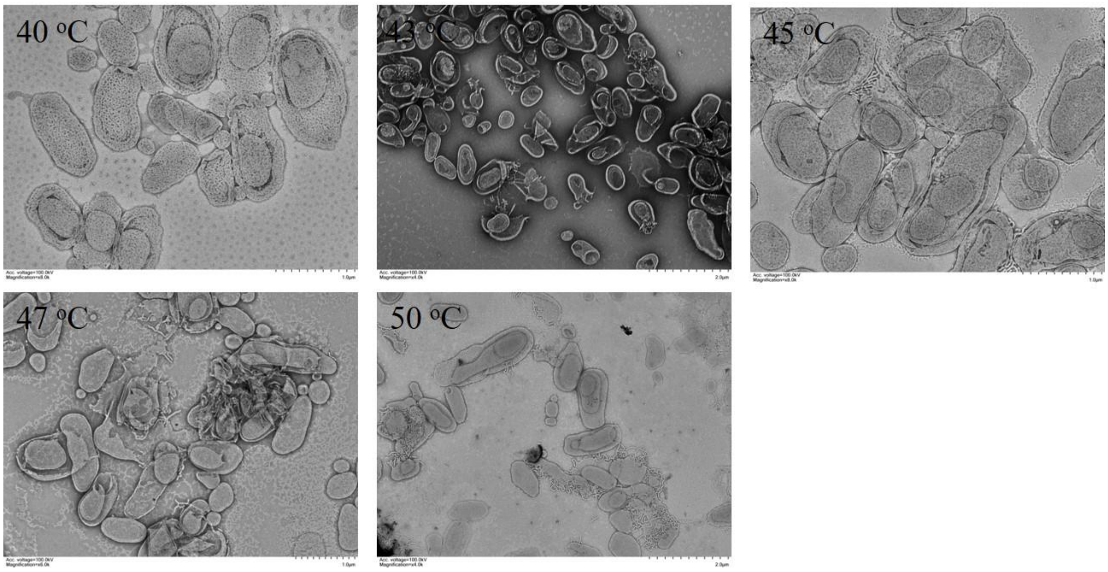

Figure S6. TEM images of mPEG$_{113}$-PHPMA$_{250}$ diblock copolymer nano-objects prepared by aqueous photo-PISA of HPMA (20% w/w HPMA concentration) using mPEG$_{113}$-CEPA as the macro-RAFT agent at different temperatures.

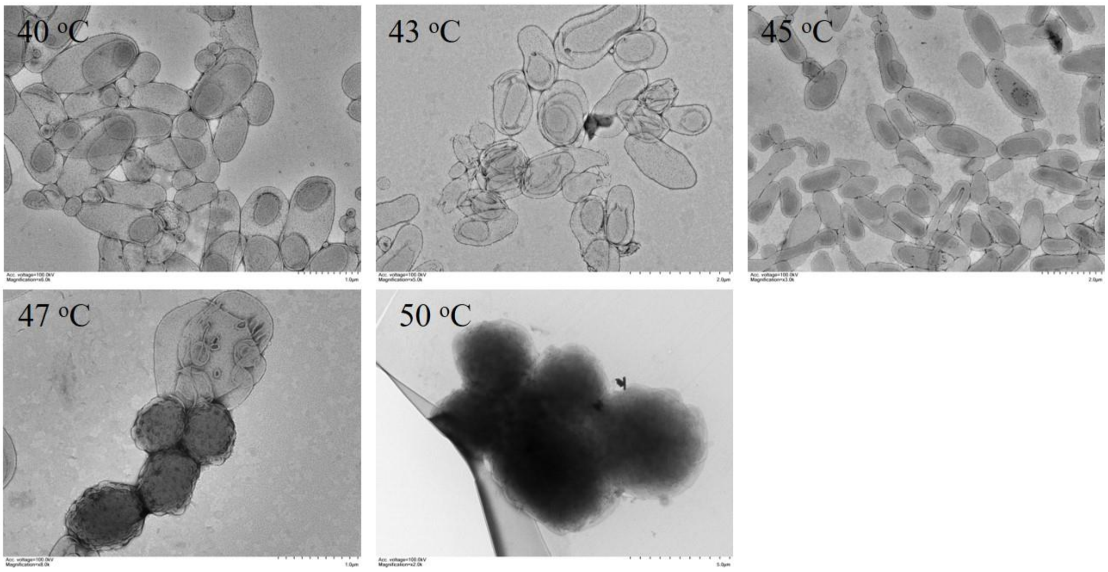

Figure S7. TEM images of mPEG$_{113}$-PHPMA$_{300}$ diblock copolymer nano-objects prepared by aqueous photo-PISA of HPMA (20% w/w HPMA concentration) using mPEG$_{113}$-CEPA as the macro-RAFT agent at different temperatures.

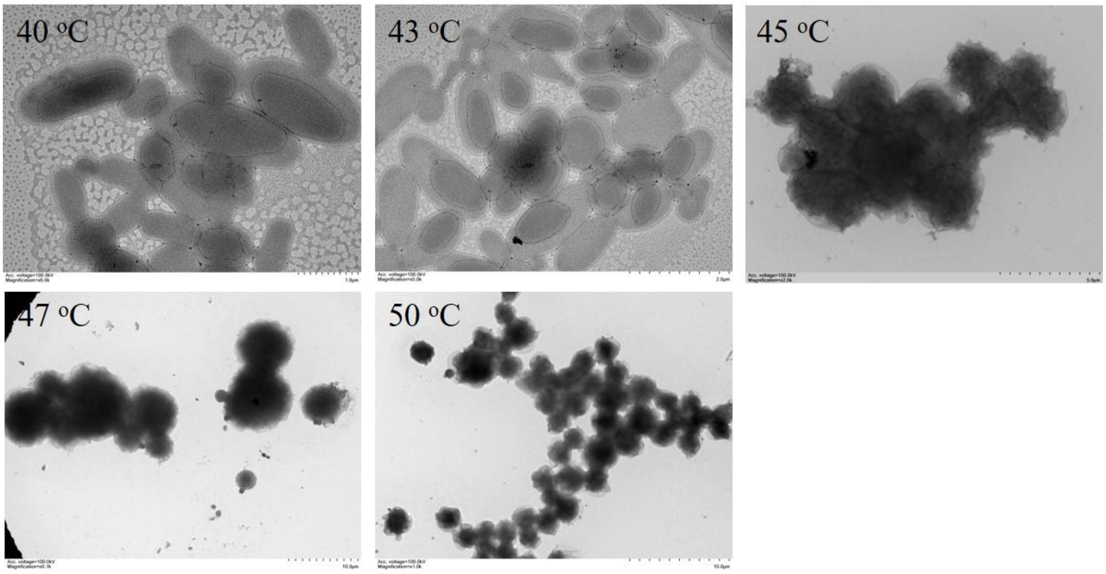

Figure S8. TEM images of mPEG$_{113}$-PHPMA$_{350}$ diblock copolymer nano-objects prepared by aqueous photo-PISA of HPMA (20% w/w HPMA concentration) using mPEG$_{113}$-CEPA as the macro-RAFT agent at different temperatures.

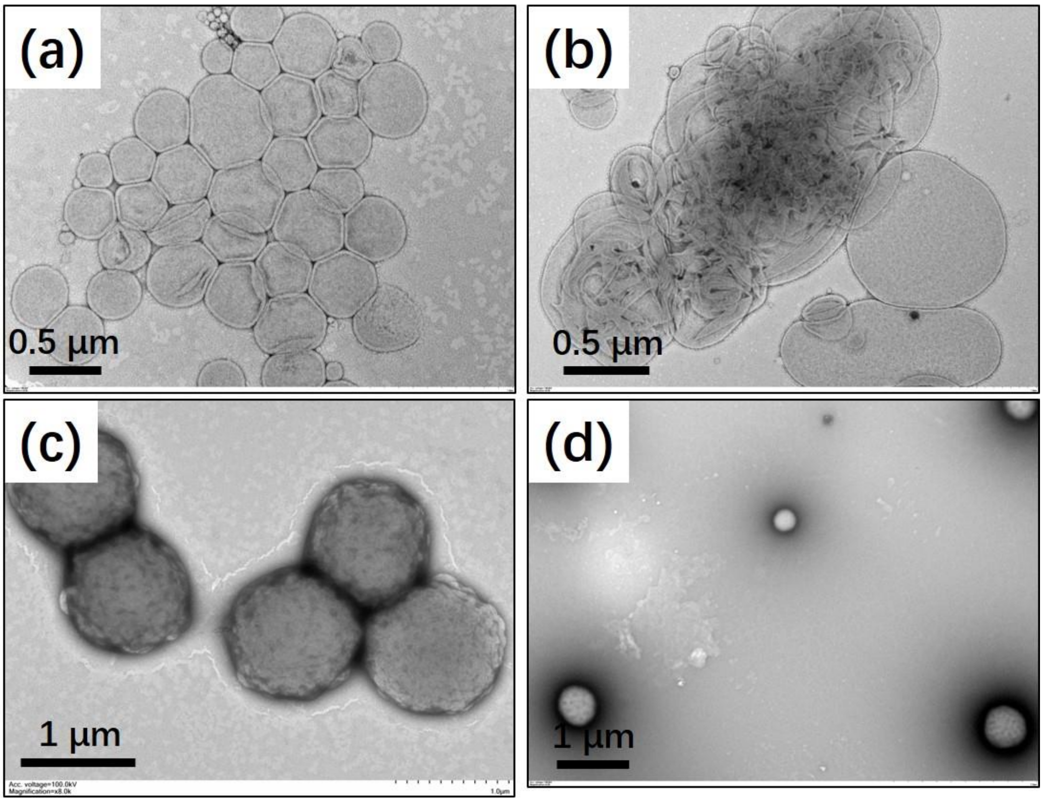

Figure S9. TEM images of mPEG$_{113}$-PHPMA$_{400}$ diblock copolymer nano-objects prepared by temperature-programmed photo-PISA of HPMA at 47 ^{o}C with different concentrations of HPMA: (a) 10% w/w, (b) 15% w/w, (c) 20% w/w, (d) 25% w/w.

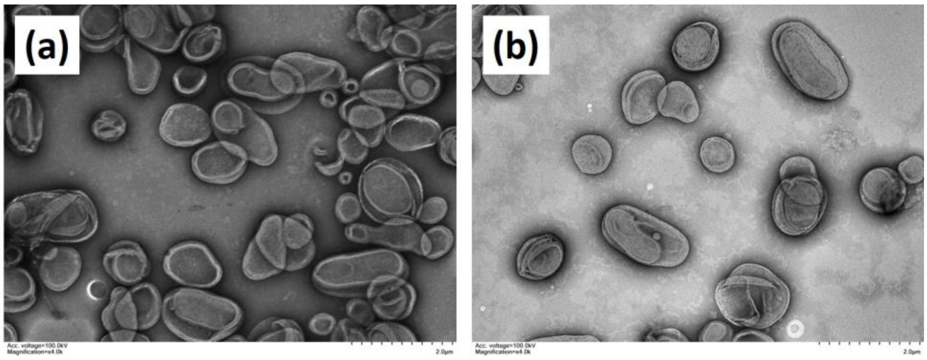

Figure S10. (a) TEM image of mPEG$_{113}$-PHPMA$_{400}$ diblock copolymer prepared by aqueous photo-PISA at 40 ^{o}C (20% w/w HPMA). (b) TEM image of the obtained sample of mPEG$_{113}$-PHPMA$_{400}$ vesicles (Figure S10a) after the incubation at 47 ^{o}C for 1 h.

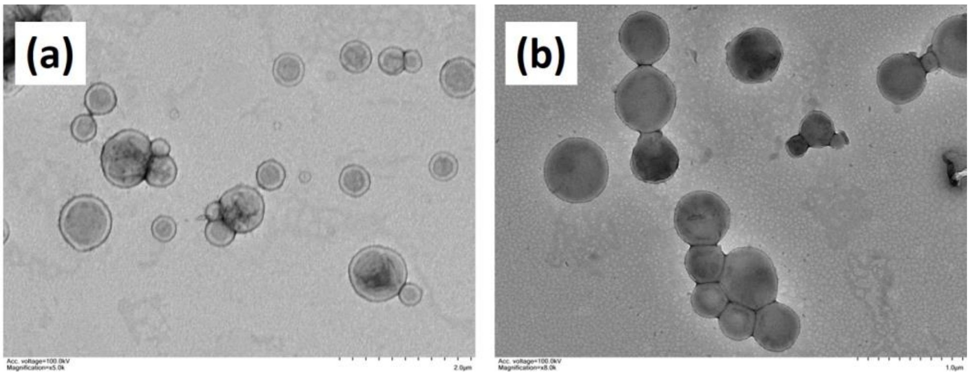

Figure S11. TEM images of PGMA$_{42}$-PHPMA$_{400}$ (GMA = glycerol monomethacrylate) diblock copolymer nano-objects prepared by aqueous photo-PISA at either (a) 40 or (b) 47 °C (20% w/w HPMA concentration).

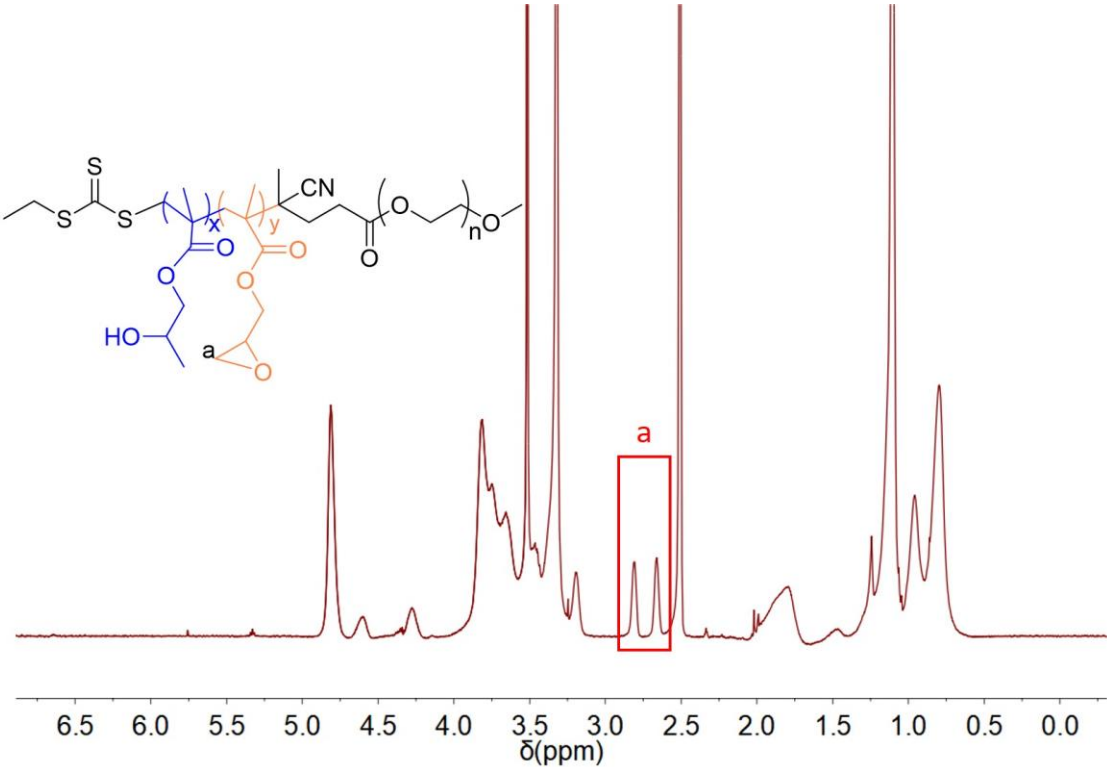

Figure S12. ^{1}H NMR spectrum of mPEG$_{113}$-P(HPMA$_{320}$-*co*-GlyMA$_{80}$) diblock copolymers prepared by aqueous photo-PISA at 47 °C with the monomer concentration of 20% w/w.

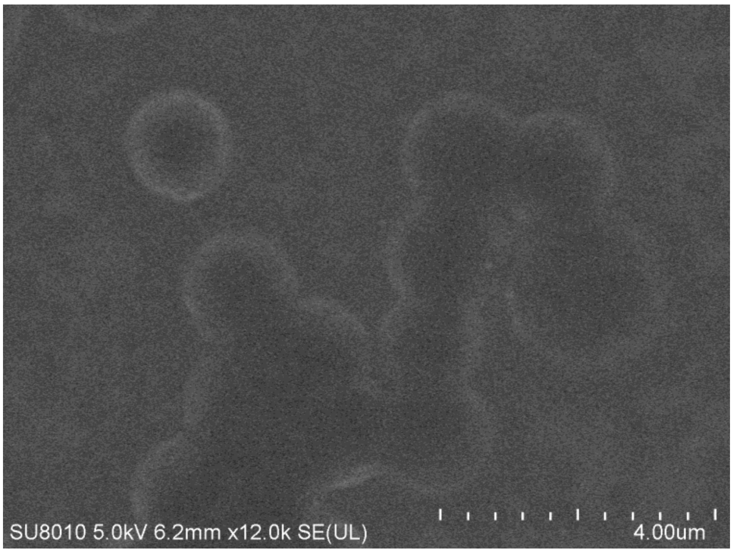

Figure S13. SEM image of mPEG$_{113}$-P(HPMA$_{320}$-*co*-GlyMA$_{80}$) LCVs.

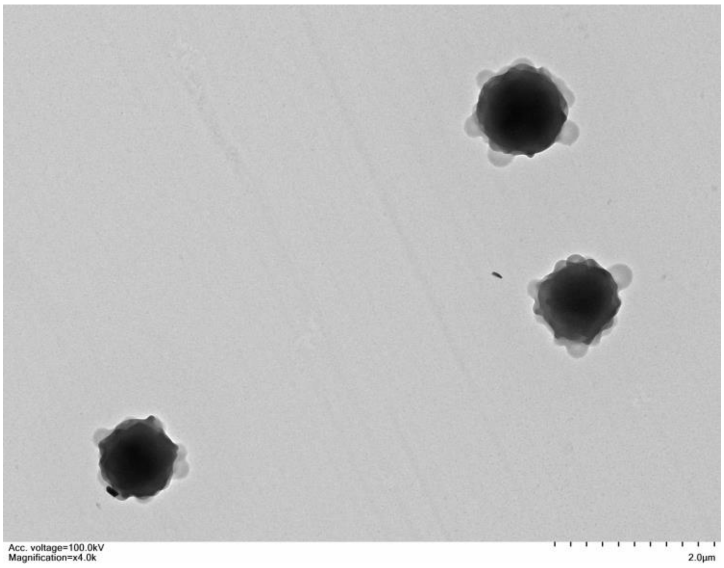

Figure S14. TEM images of cross-linked mPEG$_{113}$-P(HPMA$_{320}$-*co*-GlyMA$_{80}$) LCVs after treating with 10% w/w SDS.

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