Supporting Information for

Synthesis and micellization of multi-stimuli responsive block copolymer based on spiropyran

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Experimental

1. Materials

The monomer of *N*-isopropylacrylamide (NIPAM, >99%, Acros Organics) was purified by recrystallization in an acetone/n-hexane mixture (50:50 by volume). The monomer of *N*-acryloylglycine (NAG) was synthesized as discussed elsewhere.[1] The RAFT agent 4-cyano-4-(dodecylsulfanyl thiocarbonyl) sulfanyl pentanoic acid (CDTPA) was synthesized as discussed elsewhere.[2] 2-(3',3',5'-trimethyl-6-nitro-3'*H*-spiro[chromene-2,2'-indol]-1'-yl)-ethanol (SP-OH) was synthesized according to modified literature procedures.[3] 4-(Dimethylamino)pyridine (DMAP), *N*,*N'*-dicyclohexylcarbodiimide (DCC) and other chemical reagents were of analytic grade and were used as received. Deionized water was used in the present experiments.

2. Instruments

The ^{1}H NMR analysis was performed on a Bruker Avance III 400 MHz NMR spectrometer using DMSO or D_2O as solvent. The molecular weight and the polydispersity index (*Đ*, $Đ = M_w/M_n$) of the synthesized polymers were determined by gel permeation chromatography (GPC) equipped with an Agilent 1260 GPC system at 25 ^{0}C, where H_2O containing 0.02 wt% sodium azide was used as the eluent and the dextran with molecular weight at 40000 was used employed for calibration standard. The LCSTs of the

thermo-responsive polymers was determined by turbidity analysis at 800 nm on a Varian 100 UV-vis spectrophotometer equipped with a thermo-regulator (±0.1 ^{0}C) with the heating/cooling rate at 1 ^{0}C min^{-1}, in which the LCST value was determined at 50% change of the transmittance. Transmission electron microscopy (TEM) observation was performed using a Tecnai G^2 F20 electron microscope at an acceleration of 200 kV. UV light irradiation for the samples was carried out on a hand-held ultraviolet lamp (365 nm, 8 W nominal power). The UV-vis absorption spectra were measured using a Shimadzu UV-2101PC spectrophotometer.

3. Preparation of PNIPAM-*b*-P(NAG-*co*-NAGSP)

3.1 Synthesis of PNIPAM-trithiocarbonate macro-RAFT agent

The PNIPAM-trithiocarbonate macro-RAFT agent, PNIPAM$_{94}$-TTC in which TTC represent the RAFT terminal of trithiocarbonate, was prepared by solution RAFT polymerization of NIPAM in 1,4-dioxane at 70 ^{0}C using CDTPA as the RAFT agent and AIBN as the initiator. In a 100 mL Schlenk flask with a magnetic bar, NIPAM (10.00 g, 88.40 mmol), CDTPA (356.60 mg, 0.88 mmol), and AIBN (29.10 mg, 0.18 mmol) dissolved in 1,4-dioxane (30.00 g) were added. The solution was degassed with nitrogen at 0 ^{0}C, and then the flask content was immersed in a preheated oil bath at 70 ^{0}C for 3 h. The polymerization was quenched by rapid cooling upon immersion of the flask in iced water. The monomer conversion, 94%, was determined by ^{1}H NMR analysis. The synthesized polymer was precipitated into diethyl ether at 0 ^{0}C, collected by three precipitation/filtration cycles, and then dried at room temperature under vacuum. The PNIPAM$_{94}$-TTC macro-RAFT agent was characterized by ^{1}H NMR (Figure S1A) and GPC analysis (Figure S2A).

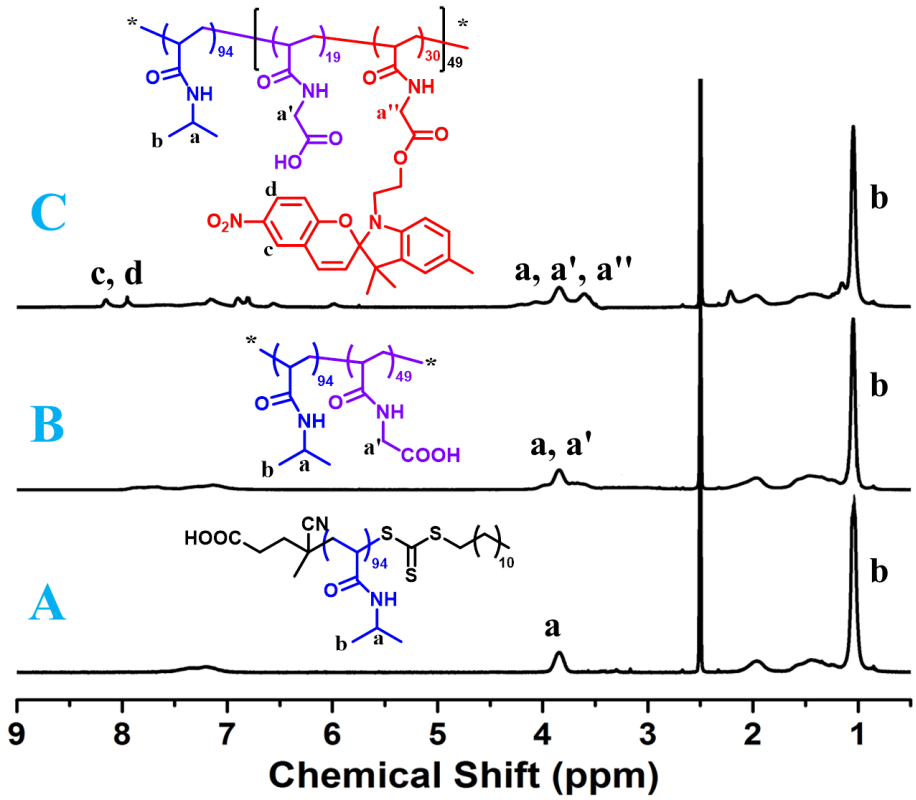

Figure S1. ^{1}H NMR spectra of PNIPAM$_{94}$-TTC (A), PNIPAM$_{94}$-*b*-PNAG$_{49}$-TTC (B), PNIPAM$_{94}$-*b*-P(NAG$_{19}$-*co*-NAGSP$_{30}$) (C).

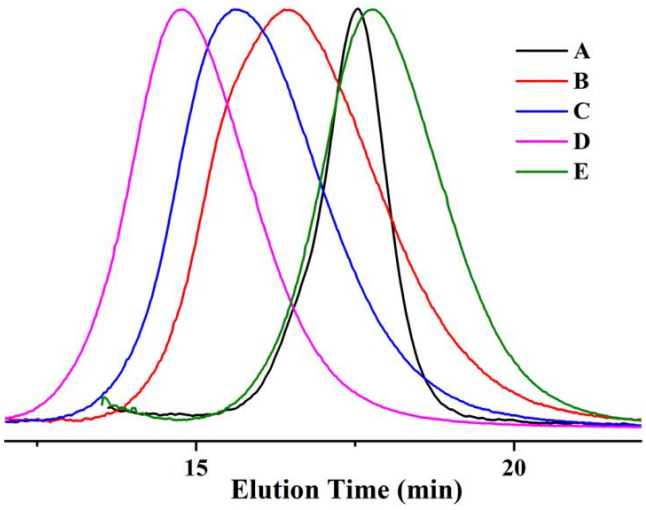

Figure S2. The GPC traces of PNIPAM$_{94}$-TTC (A), PNIPAM$_{94}$-*b*-PNAG$_{29}$-TTC (B), PNIPAM$_{94}$-*b*-PNAG$_{49}$-TTC (C), PNIPAM$_{94}$-*b*-PNAG$_{99}$-TTC (D), PNAG$_{49}$-TTC (E).

3.2 Synthesis of the PNIPAM-*b*-PNAG-TTC diblock copolymer

Three samples of the PNIPAM-*b*-PNAG-TTC diblock copolymer with a constant

DP of the PNIPAM but different DP of the PNAG block were prepared. Herein, a typical RAFT polymerization of $PNIPAM_{94}$-*b*-$PNAG_{49}$-TTC was introduced. Into a Schlenk flask with a magnetic bar, NAG (877.60 mg, 6.80 mmol), $PNIPAM_{94}$-TTC (1.50 g, 0.14 mmol), and AIBN (5.60 mg, 0.034 mmol) dissolved in 1,4-dioxane/H_2O (w/w = 3/1, 3.47 g). The flask content was degassed with nitrogen at 0 ^{0}C, and then the polymerization was performed at 70 ^{0}C under magnetically stirring. After a given time, the polymerization was quenched by rapid cooling upon immersion of the flask in iced water. To check the monomer conversion, once the polymerization was quenched, the internal standard of 1,3,5-trioxane (58.00 mg, 0.64 mmol) was added and distributed homogeneously in the polymerization mixture by vigorous stirring, and then a drop of the polymerization solution (about 0.05 mL) was diluted with D_2O (0.5 mL) and subjected to ^{1}H NMR analysis. The NAG monomer conversion was calculated by comparing the signal of NAG at δ = 5.95 ppm with the signal of 1,3,5-trioxane at δ = 5.12 ppm. The synthesized polymer of PNIPAM-*b*-PNAG-TTC was isolated by precipitation into cold diethyl ether for three times, and dried under vacuum at room temperature overnight to afford yellow powder of sample. The synthesized polymer of $PNIPAM_{94}$-*b*-$PNAG_{49}$-TTC was characterized by ^{1}H NMR analysis (Figure S1B) and GPC analysis (Figure S2B-D) and the results were summarized in Table S1.

Table S1. Experimental Details and Summary of the Synthesized Polymers of $PNIPAM_{94}$-TTC and $PNIPAM_{94}$-*b*-PNAG-TTC.

Polymer	$[M]_0$:$[CTA]_0$:$[I]_0$	Time (h)	Conv. (%)[a]	M_n (kg/mol)			$Đ$[e]
				$M_{n,th}$[b]	$M_{n,GPC}$[c]	$M_{n,NMR}$[d]	
$PNIPAM_{94}$-TTC	500:5:1	3	94	11.03	13.22	11.85	1.13
$PNIPAM_{94}$-$PNAG_{29}$-TTC	120:4:1	3	97	14.77	23.41	16.29	1.14
$PNIPAM_{94}$-$PNAG_{49}$-TTC	200:4:1	3	99	17.35	27.07	19.06	1.19
$PNIPAM_{94}$-$PNAG_{99}$-TTC	400:4:1	3	99	23.80	37.56	26.89	1.28

[a] The monomer conversion determined by ^{1}H NMR analysis.

[b] Theoretical molecular weight determined by monomer conversion.

[c] The molecular weight determined by GPC analysis.

[d] The molecular weight determined by ^{1}H NMR analysis.

[e] The $Đ$ (M_w/M_n) value determined by GPC analysis.

3.3 Synthesis of PNIPAM-*b*-P(NAG-*co*-NAGSP)

Five samples of PNIPAM-*b*-P(NAG-*co*-NAGSP) containing a constant DP of the PNIPAM but different DP of the P(NAG-*co*-NAGSP) block or different SP fraction were prepared. Herein, a typical synthesis of $PNIPAM_{94}$-*b*-$P(NAG_{19}$-*co*-$NAGSP_{30})$ was introduced. $PNIPAM_{94}$-*b*-$PNAG_{49}$-TTC (400.00 mg, 1.15 mmol equiv of -COOH), 2-(3',3',5'-trimethyl-6-nitro-3'*H*-spiro[chromene-2,2'-indol]-1'-yl)-ethanol (SP-OH) (422.00 mg, 1.15 mmol -OH) and DMAP (14.10 mg, 0.12 mmol) were dissolved in DMF (5 mL), and finally DCC (237.50 mg, 1.20 mmol) was added to the reaction mixture. The solution was stirred at room temperature for 48 h and was then filtered to remove any DCC-urea side product and then precipitated into iced diethyl ether/n-hexane (v/v = 4:1) for three times, the product was dried to afford a light pink powder sample. The ^{1}H NMR spectra of $PNIPAM_{94}$-*b*-$P(NAG_{19}$-*co*-$NAGSP_{30})$ was shown in Figure S1C. The quantitative conversion of the -COOH was confirmed by ^{1}H NMR spectroscopy with the protons at 8.00 ppm and 1.02 ppm (Figure S1C). Five samples of PNIPAM-*b*-P(NAG-*co*-NAGSP) with different chemical composition were summarized in Table S2.

Table S2. Summary of the PNIPAM-*b*-P(NAG-*co*-NAGSP) block copolymers..

Polymer	SP fraction (PNAGSP/(PNAG+PNAGSP))
$PNIPAM_{94}$-*b*-$P(NAG_{12}$-*co*-$NAGSP_{17})$	60%
$PNIPAM_{94}$-*b*-$P(NAG_{19}$-*co*-$NAGSP_{30})$	60%
$PNIPAM_{94}$-*b*-$P(NAG_{36}$-*co*-$NAGSP_{13})$	26%
$PNIPAM_{94}$-*b*-$P(NAG_{28}$-*co*-$NAGSP_{21})$	43%
$PNIPAM_{94}$-*b*-$P(NAG_{52}$-*co*-$NAGSP_{47})$	47%

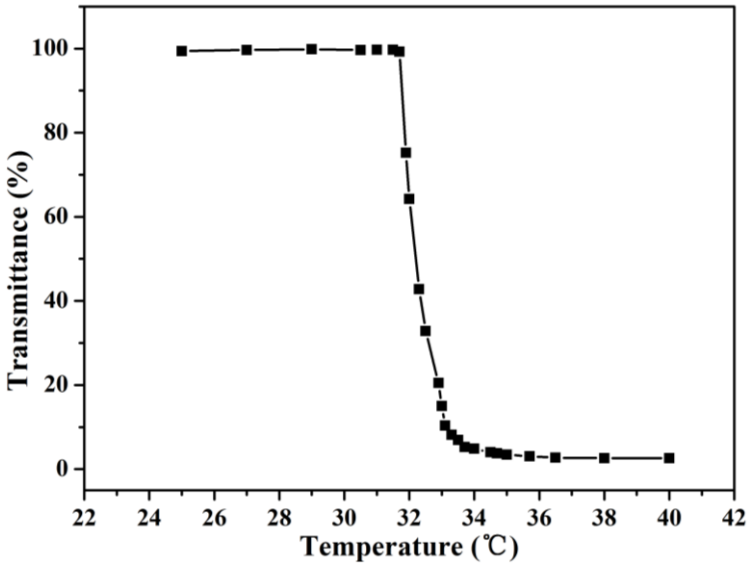

Figure S3. The temperature dependent transmittance of the 0.10 wt% aqueous solution of the $PNIPAM_{94}$-TTC.

4. Preparation of P(NAG-*co*-NAGSP)

4.1 Synthesis of PNAG-TTC

The PNAG-TTC was prepared by solution RAFT polymerization of NAG in 1,4-dioxane/H_2O (w/w = 3/1) at 70 ^{0}C using CDTPA as the RAFT agent and AIBN as the initiator. In a 100 mL Schlenk flask with a magnetic bar, NAG (3.00 g, 23.26 mmol), CDTPA (187.40 mg, 0.47 mmol), the internal standard of 1,3,5-trioxane (32.60 mg, 0.36 mmol) and AIBN (19.00 mg, 0.12 mmol) dissolved in 1,4-dioxane/H_2O (6.97 g) were added. The solution was degassed with nitrogen at 0 ^{0}C, and then the flask content was immersed in a preheated oil bath at 70 ^{0}C for 3h. The polymerization was quenched by rapid cooling upon immersion of the flask in iced water. The monomer conversion was determined by ^{1}H NMR analysis by comparing the integral areas of the monomer protons δ = 5.95 ppm with those of the 1,3,5-trioxane internal standard at δ = 5.12 ppm.. The synthesized polymer was precipitated into diethyl ether at 0 ^{0}C, collected by three precipitation/filtration cycles, and then dried at room temperature under vacuum. The PNAG-TTC was characterized by GPC analysis analysis, Đ = 1.21 (Figure S2E) and ^{1}H NMR (Figure S4A).

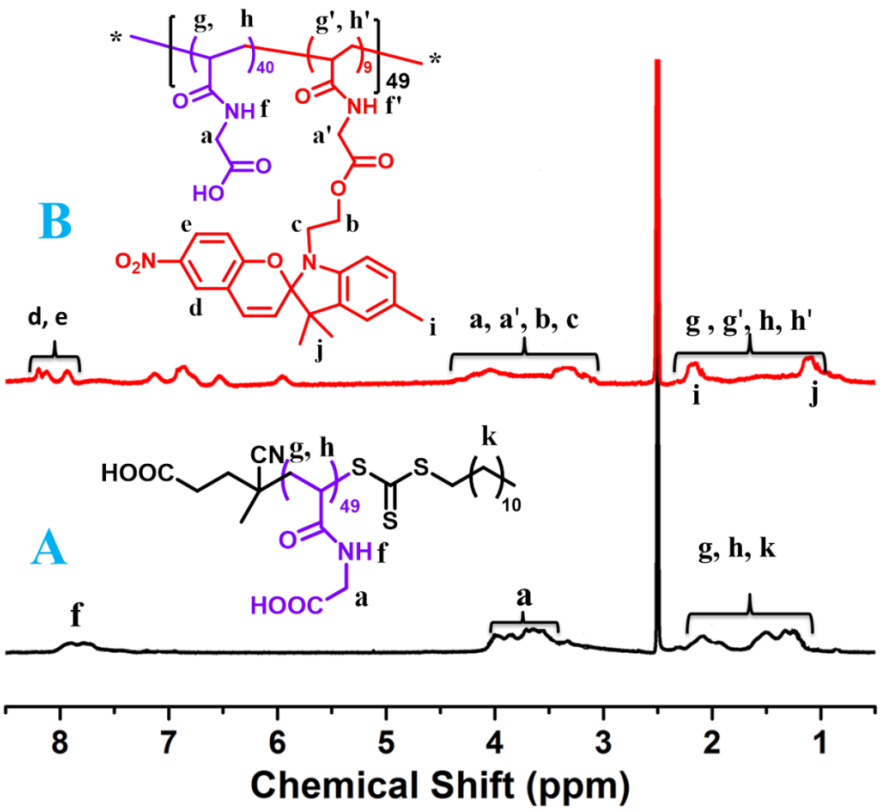

Figure S4. ^{1}H NMR spectra of PNAG$_{49}$-TTC (A) and P(NAG$_{40}$-*co*-NAGSP$_{9}$) (B).

4.2 Synthesis of P(NAG$_{40}$-*co*-NAGSP$_{9}$)

P(NAG$_{40}$-*co*-NAGSP$_{9}$) is synthesized through modification of the pre-prepared homopolymer PNAG-TTC with SP. PNAG$_{49}$-TTC (400.00 mg, 2.97 mmol equiv of -COOH), 2-(3',3',5'-trimethyl-6-nitro-3'*H*-spiro[chromene-2,2'-indol]-1'-yl)-ethanol (SP-OH) (326.50 mg, 0.89 mmol -OH) and DMAP (10.90 mg, 0.09 mmol) were dissolved in DMF (10 mL), and finally DCC (183.70 mg, 0.89 mmol) was added to the reaction mixture. The solution was stirred at room temperature for 48 h and was then filtered to remove any DCC-urea side product and then precipitated into iced diethyl ether/n-hexane (v/v = 4:1) for three times, the product was dried to afford a light pink powder sample. The ^{1}H NMR of P(NAG$_{40}$-*co*-NAGSP$_{9}$) was shown in Figure S4B. The quantitative conversion of the -COOH was confirmed by ^{1}H NMR spectroscopy with the protons of SP at 8.00 ppm and those of P(NAG$_{40}$-*co*-NAGSP$_{9}$) (a, a', b, c) at 3.00-4.05 ppm (Figure S4B).

5. Characterizations

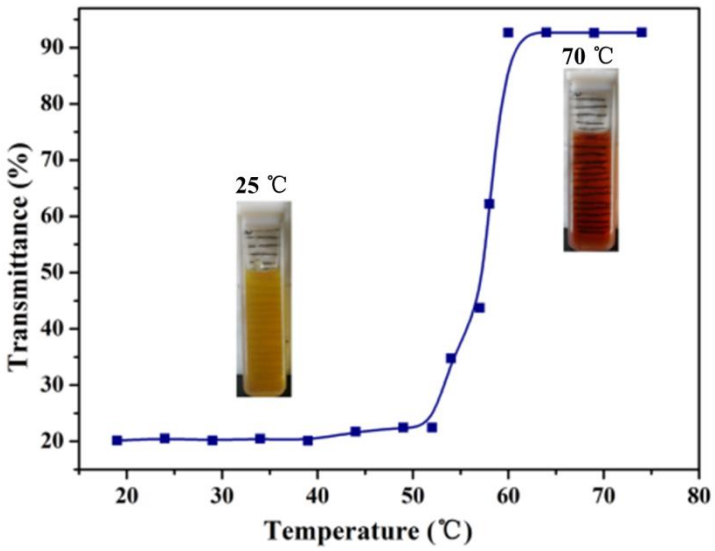

Figure S5. The temperature dependent transmittance of 0.1 wt% aqueous dispersions of P(NAG_{40}-*co*-$NAGSP_9$). The insets show the photographs of aqueous dispersions of P(NAG_{40}-*co*-$NAGSP_9$) at 25 and 70 ^{0}C.

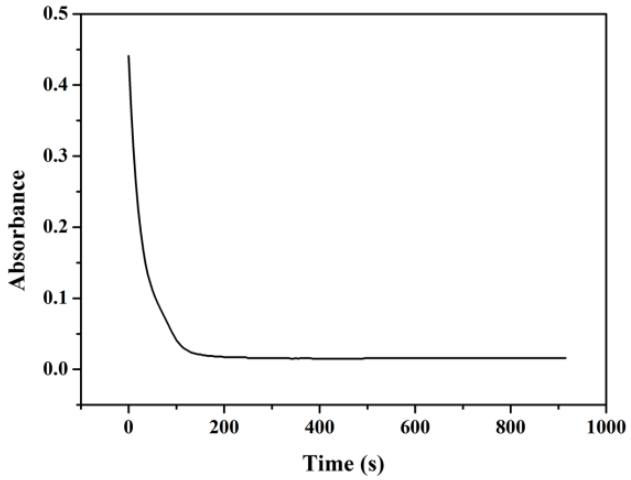

Figure S6. The time-dependent absorbance of the SP-OH solution (0.10 mmol/L, dissolved in $CHCl_3$) at 550 nm just after the SP-OH solution being irradiated with 365 nm UV light for 5 min.

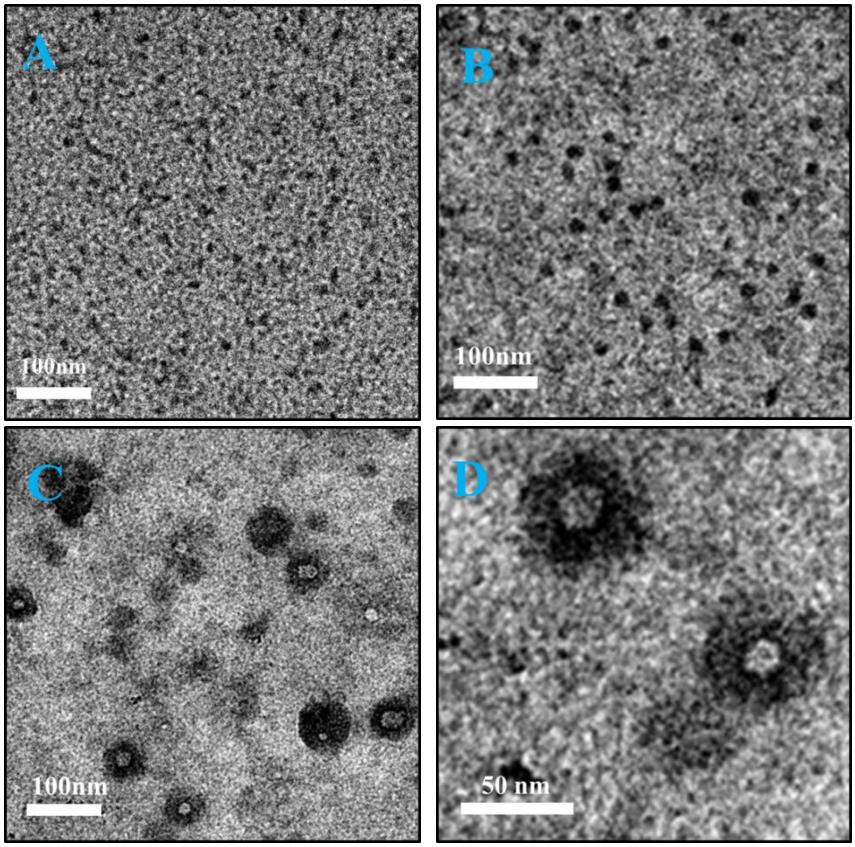

Figure S7. TEM images of the PNIPAM$_{94}$-*b*-P(NAG$_{12}$-*co*-NAGSP$_{17}$) (A), PNIPAM$_{94}$-*b*-P(NAG$_{28}$-*co*-NAGSP$_{21}$) (B), PNIPAM$_{94}$-*b*-P(NAG$_{52}$-*co*-NAGSP$_{47}$) (C) and PNIPAM$_{94}$-*b*-P(NAG$_{52}$-*co*-NAGSP$_{47}$) micelles (D) at 25 ^{0}C.

References

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