Supporting Information for

Enzyme-responsive polymeric micelles with fluorescence fabricated through aggregation-induced copolymer self-assembly for anticancer drug delivery

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FBS (10%, v/v) for 5 days.

Fig. S8 TEM of CH_3O-PEG_{43}-*b*-PAA_{55} in water.

Fig. S9 The DOX release of DOX@CH_3O-PEG_{43}-*b*-P(AA_{20}-*g*-TPE_{35}) at pH 5.0 in the presence of esterase (200 U/L) was recorded by using fluorescence spectra. Additionally, 485 nm of exciting wavelength was adopted.

S1 Experimental Section

S1.1 Synthesis of CH_3O-PEG_{43}-Br

After 20 g of CH_3O-PEG_{43}-OH was dissolved in 150 mL of toluene, approximately 40 mL of toluene with traces of water was removed from the mixture by zeotropic distillation at reduced pressure. Then 2.500 mL of Triethylamine was added into the solution at 0 °C. Subsequently, 2.470 mL of 2-bromoisobutyryl bromide was added dropwise via a constant pressure funnel during 40 min with magnetic stirring, and the reaction was performed with moderate stirring overnight at room temperature. After most toluene was removed at reduced pressure, the product was precipitated in excess cold ether. The precipitate was dried under vacuum, dissolved in 20 mL of pH 8-9 $NaHCO_3$ aqueous solution, and extracted with CH_2Cl_2. Subsequently, the organic phase was gathered and dried over $MgSO_4$. Finally, CH_2Cl_2 was removed completely at reduced pressure to obtain the resultant macroinitiator (CH_3O-PEG_{43}-Br).

S1.2 Synthesis of CH_3O-PEG_{43}-*b*-P*t*BA_{55}

CH_3O-PEG_{43}-*b*-P*t*BA_{55} was synthesized via the ATRP of *tert*-butyl acrylate (*t*BA) with the macroinitiator CH_3O-PEG_{43}-Br. An amount of 1.830 g (0.880 mM) of CH_3O-PEG_{43}-Br was dissolved in 6 mL of anhydrous tetrahydrofuran (THF). After the mixture was gassed and degassed under N_2, 0.173 g (0.880 mM) of *N,N,N′,N″,N″*-pentamethyl diethylenetriamine and 9.580 mL of *t*BA were charged under degassing by freeze-pump-thaw in a N_2 atmosphere, followed by adding 0.127 g (0.880 mM) of CuBr and then degassing. Subsequently, ATRP was carried out at 45 °C for 8 h with the conversion of *t*BA of 100% from the information on ^{1}H NMR analysis. The copper catalyst in the resultant solution was removed with an alumina column, after dilution with THF. The block copolymer CH_3O-PEG_{43}-*b*-P*t*BA_{55} was precipitated in cold ether and dried in vacuum overnight at room temperature.

S1.3 Hydrolysis of CH_3O-PEG_{43}-*b*-P*t*BA_{55}

The triblock copolymer was dissolved in 25 mL of CH_2Cl_2, and 4 mL of TFA was added and stirred at room temperature for 24 h. Most of the CH_2Cl_2 and TFA were removed at reduced pressure by a

rotary evaporator. The hydrolytic copolymers of CH_3O-PEG_{43}-*b*-PAA_{55} were obtained by lyophilization for 6 h.

S2 Supplementary Figures

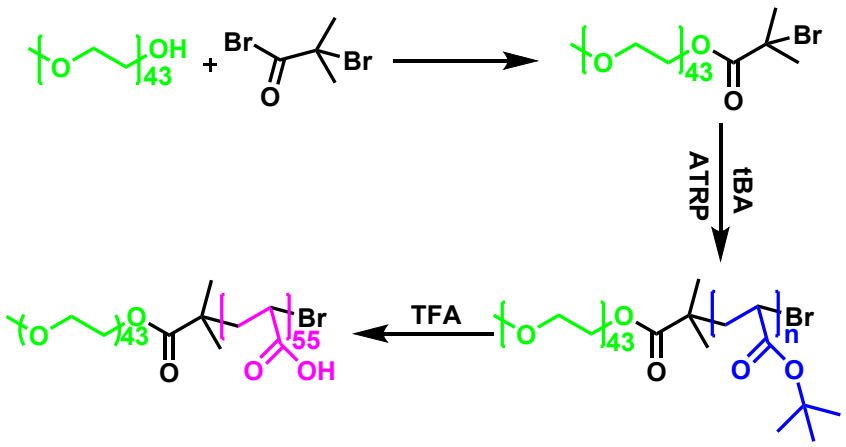


Fig. S1 Synthetic process of the CH_3O-PEG_{43}-*b*-PAA_{55} copolymer.

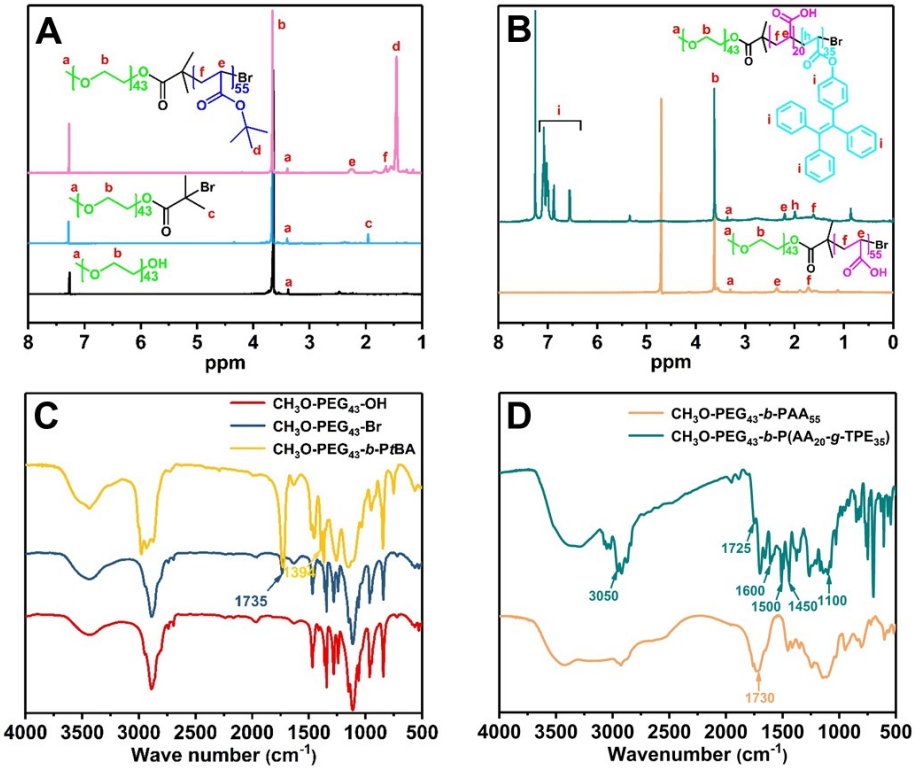


Fig. S2 (A and B) ^{1}H NMR spectra of CH_3O-PEG_{43}-OH, CH_3O-PEG_{43}-Br, and CH_3O-PEG_{43}-*b*-P*t*BA_{55}, CH_3O-PEG_{43}-*b*-PAA_{55} and CH_3O-PEG_{43}-*b*-P(AA_{20}-*g*-TPE_{35}). (C and D) FT-IR spectra of CH_3O-PEG_{43}-OH, CH_3O-PEG_{43}-Br, and CH_3O-PEG_{43}-*b*-P*t*BA_{55}, CH_3O-PEG_{43}-*b*-PAA_{55}, CH_3O-PEG_{43}-*b*-P(AA_{20}-*g*-TPE_{35}).

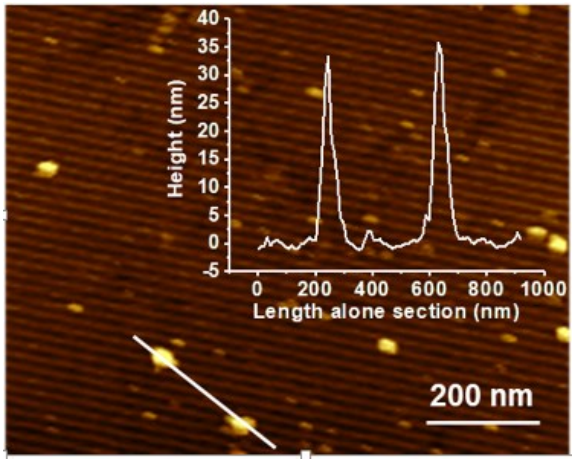


Fig. S3 AFM of CH_3O-PEG_{43}-*b*-P(AA_{20}-*g*-TPE_{35}).

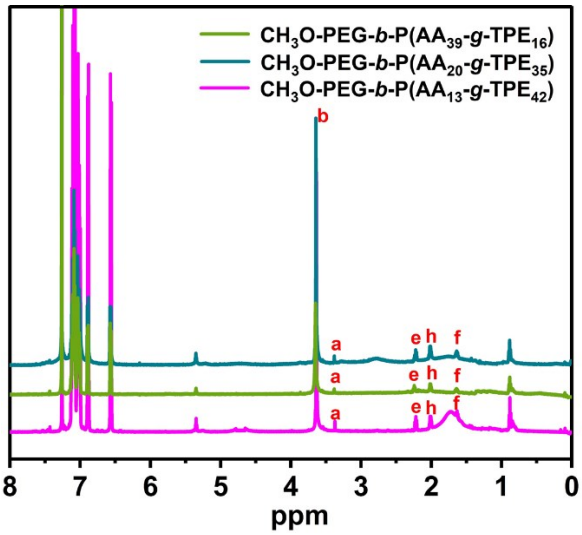


Fig. S4 ^{1}H NMR spectra of CH_3O-PEG_{43}-*b*-P(AA_{39}-*g*-TPE_{16}), CH_3O-PEG_{43}-*b*-P(AA_{20}-*g*-TPE_{35}), and CH_3O-PEG_{43}-*b*-P(AA_{13}-*g*-TPE_{42}).

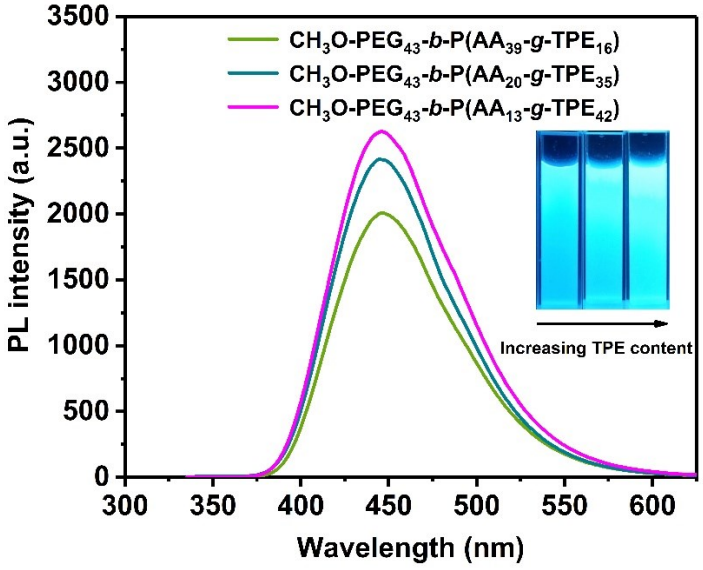


Fig. S5 Photoluminescence spectra of CH_3O-PEG_{43}-*b*-P(AA_{39}-*g*-TPE_{16}), CH_3O-PEG_{43}-*b*-P(AA_{20}-*g*-TPE_{35}), and CH_3O-PEG_{43}-*b*-P(AA_{13}-*g*-TPE_{42}) in water. Additionally, the insets are the

photographs of CH_3O-PEG_{43}-*b*-P(AA_{39}-*g*-TPE_{16}), CH_3O-PEG_{43}-*b*-P(AA_{20}-*g*-TPE_{35}), and CH_3O-PEG_{43}-*b*-P(AA_{13}-*g*-TPE_{42}) under UV lamp at 365 nm.

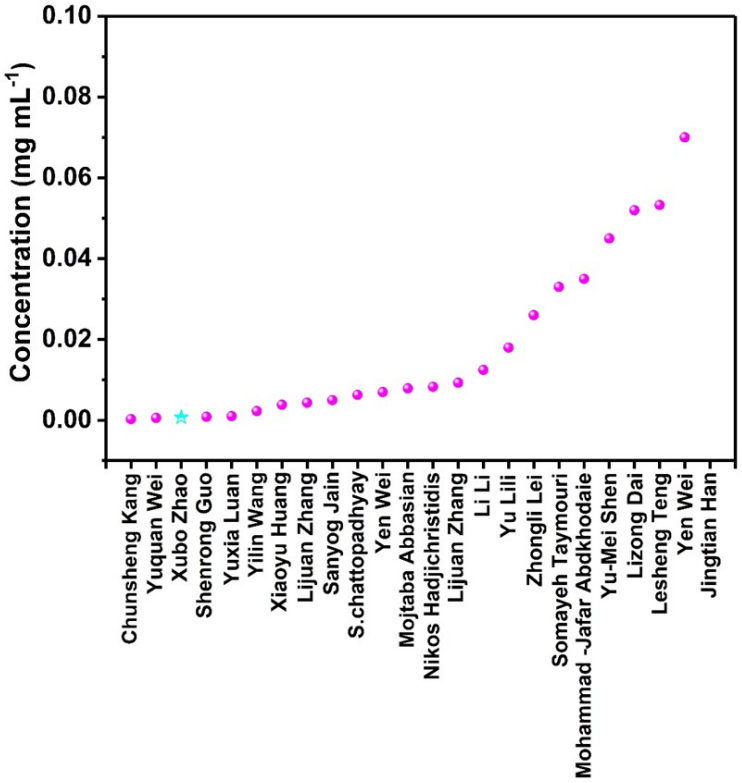


Fig. S6 CMCs of different polymeric micelles.

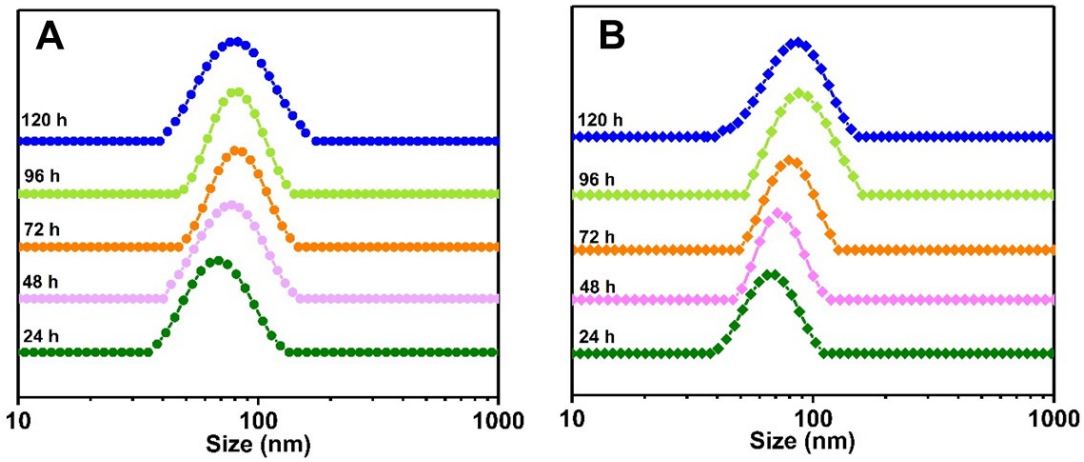
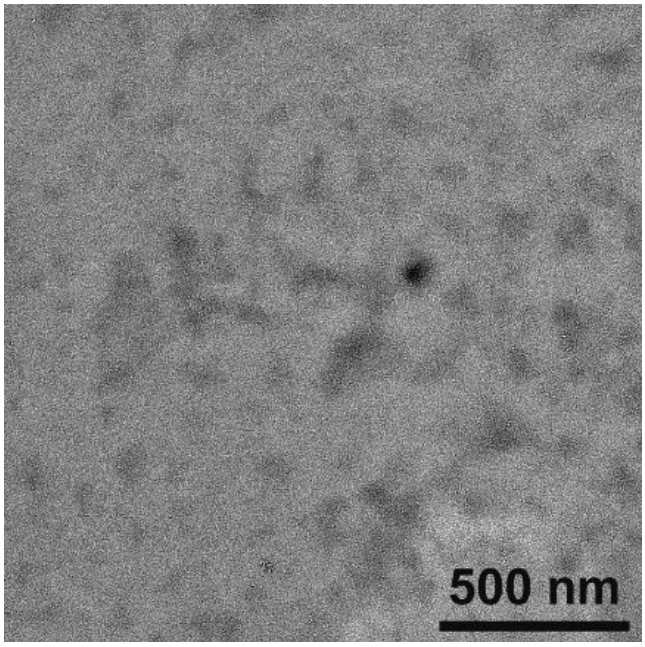


Fig. S7 Structural stability of CH_3O-PEG_{43}-*b*-P(AA_{20}-*g*-TPE_{35}) in PBS (A) and DMEM (B) with FBS (10%, v/v) for 5 days.



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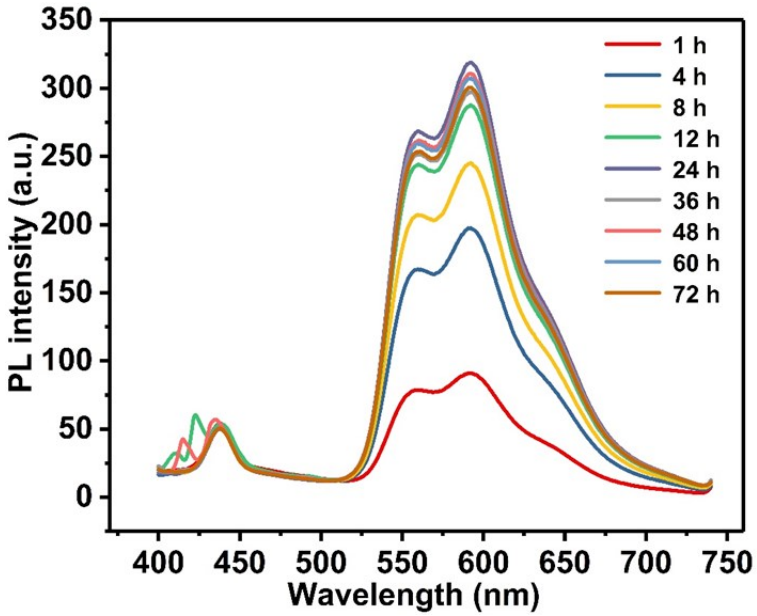

Fig. S9 The DOX release of DOX@CH_3O-PEG_{43}-*b*-P(AA_{20}-*g*-TPE_{35}) at pH 5.0 in the presence of esterase (200 U/L) was recorded by using fluorescence spectra. Additionally, 485 nm of exciting wavelength was adopted.