Supporting Information for

Aqueous Self-Assembly of Block Copolymers to Form Manganese Oxide-Based Polymeric Vesicles for Tumor Microenvironment-Activated Drug Delivery

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S1 Experimental Section

S1.1 Synthesis of Br–PEG$_{86}$–Br

After 10.0 g of HO–PEG$_{86}$–OH was dissolved in 150 mL of toluene, approximately 40 mL of toluene with traces of water was removed from the mixture by a zeotropic distillation at reduced pressure. Then 2.5 mL of Triethylamine was added into the solution at 0 °C. Subsequently, 2.0 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 (Br–PEG$_{86}$–Br).

S1.2 Synthesis of P*t*BA$_{68}$–*b*–PEG$_{86}$–*b*–P*t*BA$_{68}$

P*t*BA$_{68}$–*b*–PEG$_{86}$–*b*–P*t*BA$_{68}$ was synthesized via the ATRP of *Tert*-butyl acrylate (*t*BA) with the macroinitiator Br–PEG$_{86}$–Br. An amount of 2.080 g (0.5 mM) of Br–PEG$_{86}$–Br was dissolved in 6 mL of anhydrous Tetrahydrofuran (THF). After the mixture was gassed and degassed under N_2, 0.172g (1.0 mM) of *N,N,N″,N″*-Pentamethyl diethylenetriamine and 17.920 g (140 mM) of *t*BA were charged under degassing by freeze-pump-thaw in a N_2 atmosphere, followed by adding 0.143 g (0.1 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 P*t*BA$_{68}$–*b*–PEG$_{86}$–*b*–P*t*BA$_{68}$ was precipitated in cold ether and dried in vacuum overnight at room temperature.

S1.3 Hydrolysis of P*t*BA$_{68}$–*b*–PEG$_{86}$–*b*–P*t*BA$_{68}$

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 PAA$_{68}$–*b*–PEG$_{86}$–*b*–PAA$_{68}$ were obtained by lyophilization for 6 h.

S2 Supplementary Figures

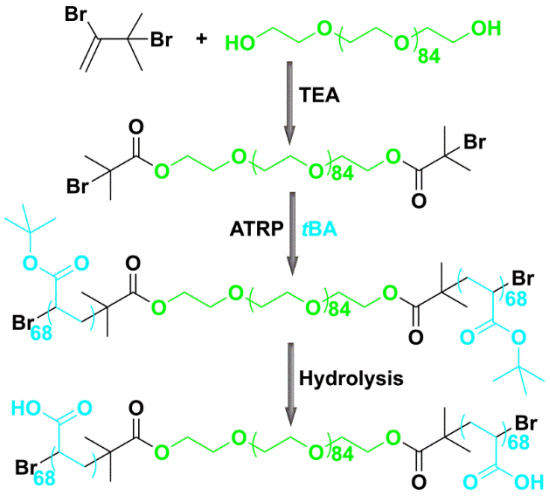

Fig. S1 Synthetic process of the PAA$_{68}$–*b*–PEG$_{86}$–*b*–PAA$_{68}$ copolymer

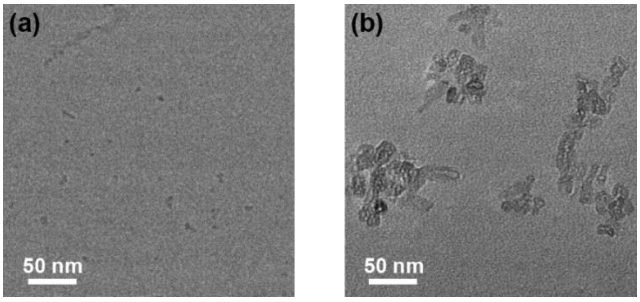

Fig. S2 TEM images of MnO_2-polymer hybrids. Images of (**a**) and (**b**) respectively corresponds to the feed concentrations of $MnCl_2$•$4H_2O$ at 1 and 3 mg mL^{-1}

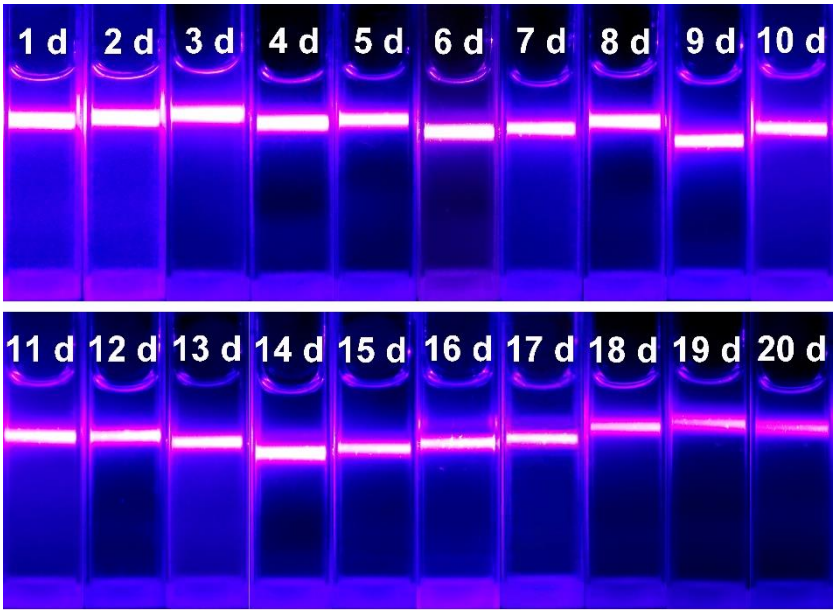

Fig. S3 Tyndall effects for structural stability of PAA_{68}–*b*–PEG_{86}–*b*–PAA_{68}/MnO_2 (1 mg mL^{-1}) in PBS for 20 days

Fig. S4 Tyndall effects for structural stability of PAA_{68}–*b*–PEG_{86}–*b*–PAA_{68}/MnO_2 (1 mg mL^{-1}) in DMEM with FBS (10%, v/v) for 6 days

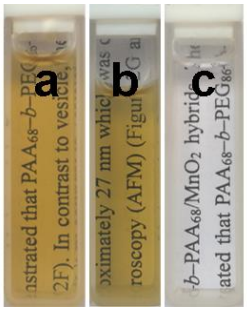

Fig. S5 Photo images for dispersed stability of PAA_{68}–*b*–PEG_{86}–*b*–PAA_{68}/MnO_2 in PBS for 1 h (**a**) and 100 days (**b**). Photo image for dissociation of PAA_{68}–*b*–PEG_{86}–*b*–PAA_{68}/MnO_2 in the presence of 10 mM GSH at pH 5.0 (**c**)

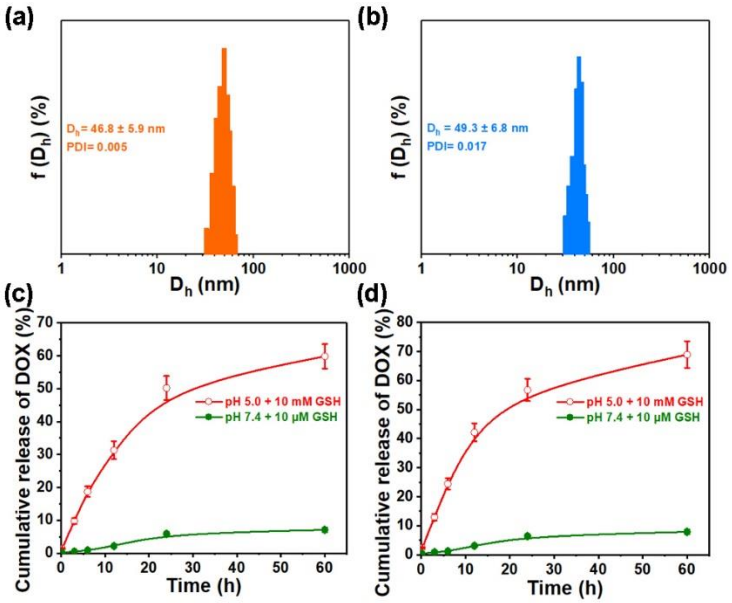

Fig. S6 D_h distributions of DOX_1-loaded PAA_{68}–*b*–PEG_{86}–*b*–PAA_{68}/MnO_2 (**a**) and DOX_2-loaded PAA_{68}–*b*–PEG_{86}–*b*–PAA_{68}/MnO_2 (**b**). The cumulative release of DOX from DOX_1-loaded PAA_{68}–*b*–PEG_{86}–*b*–PAA_{68}/MnO_2 (**c**) and DOX_2-loaded PAA_{68}–*b*–PEG_{86}–*b*–PAA_{68}/MnO_2 in simulated body fluids (**d**)

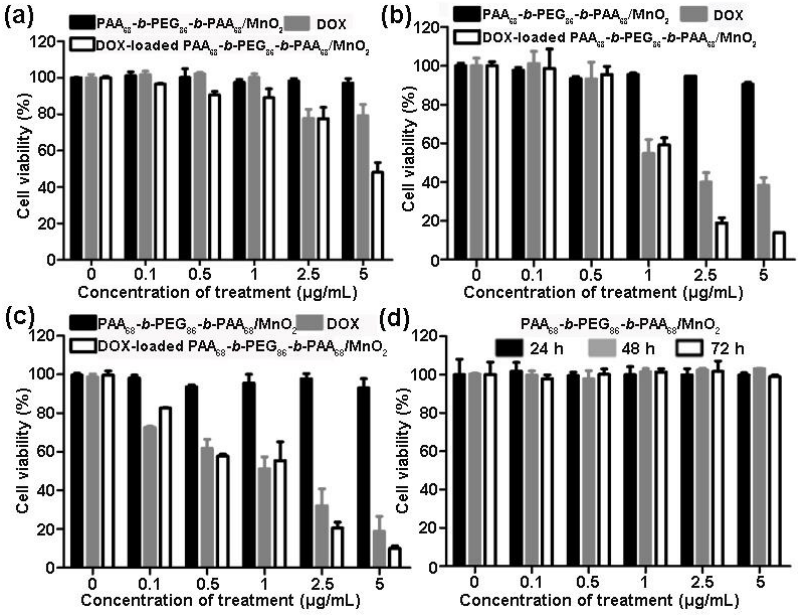

Fig. S7 Cell viability assay in MCF-7 cells by treatment with PAA_{68}–*b*–PEG_{86}–*b*–PAA_{68}/MnO_2, free DOX, and DOX-loaded PAA_{68}–*b*–PEG_{86}–*b*–PAA_{68}/MnO_2 for 24 h (**a**), 48 h (**b**), and 72 h (**c**). Additionally, Cell viability assay in HEK-293 cells by treatment with PAA_{68}–*b*–PEG_{86}–*b*–PAA_{68}/MnO_2 for different time (**d**)