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Supporting Information

Mitochondria-targeted delivery of doxorubicin and evodiamine for treatment of metastatic breast cancer

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Supplementary Figure Captions:

Fig. S1. ^{1}H NMR spectrum of TPP-COOH in DMSO-d6.

Fig. S2. ^{1}H NMR spectrum of TPP-Dex in DMSO-d6.

Fig. S3. ^{1}H NMR spectrum of SPCL in DMSO-d6.

Fig. S4. ^{1}H NMR spectrum of TPP-Dex-ss-SPCL in DMSO-d6.

Fig. S5. Zata potential of the mitochondrial-targeted stimulus-responsive copolymers TPP-Dex-ss-SPCL.

Fig. S6. A) Change in size distribution of TPP-Dex-ss-SPCL micelles in the presence of 10 μM GSH in ABS at pH 5.0; B) Changes in size distribution of TPP-Dex-ss-SPCL micelles triggered by 10 mM GSH at pH 7.4.

Fig. S7. The critical micelle concentration (CMC) of the TPP-Dex-ss-SPCL micelles at A) pH 7.5 or B) pH 5.0 condition derived from the plot of I339 /I333 ratio vs. copolymer concentration using pyrene as the probe.

Fig. S8. Size changes of micelles after incubation in PBS (pH 7.4) or in cell culture medium (containing 10 % FBS, v/v) at 37℃ for 5 days.

Fig. S9. Cytotoxicity of 4T1 cells treated by free drugs and drugs-loaded micelles as a function of DOX concentration (n = 3).

Fig. S10. Wound-healing assays showing that EVO inhibit the migration of 4T1 cells.

Table-S1. Characterizations of all the micelles.

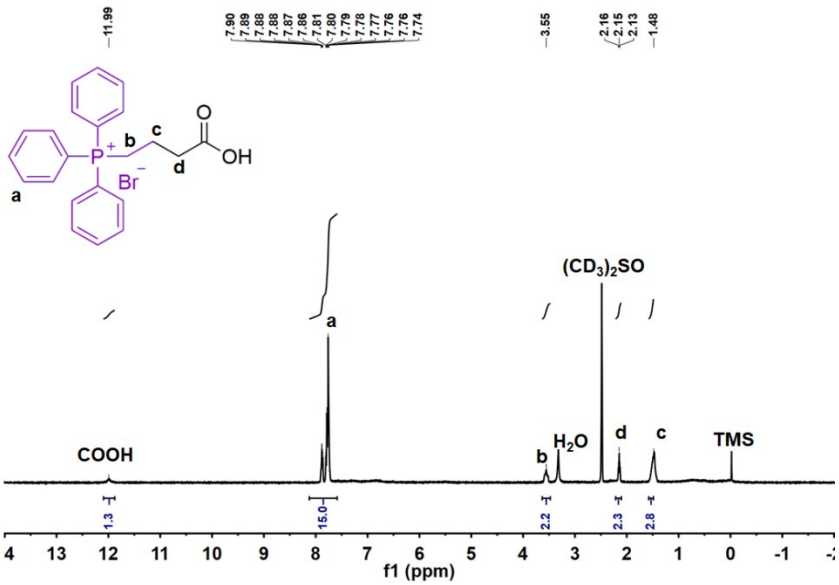


Fig. S1. [1]H NMR spectrum of TPP-COOH in DMSO-d6.

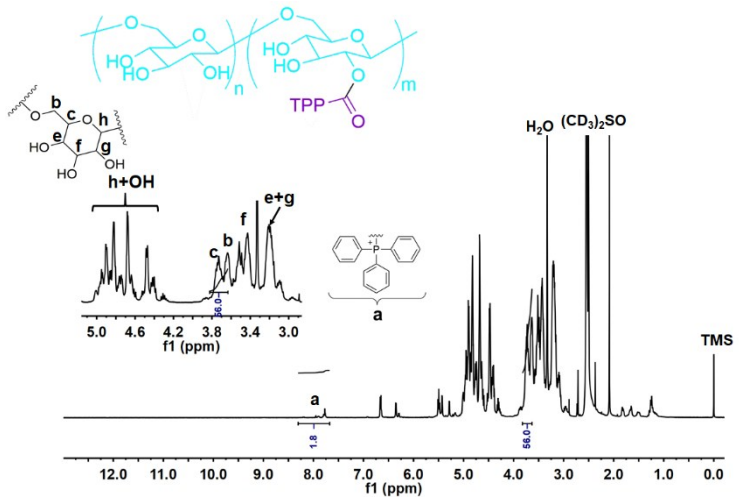


Fig. S2. [1]H NMR spectrum of TPP-Dex in DMSO-d6.

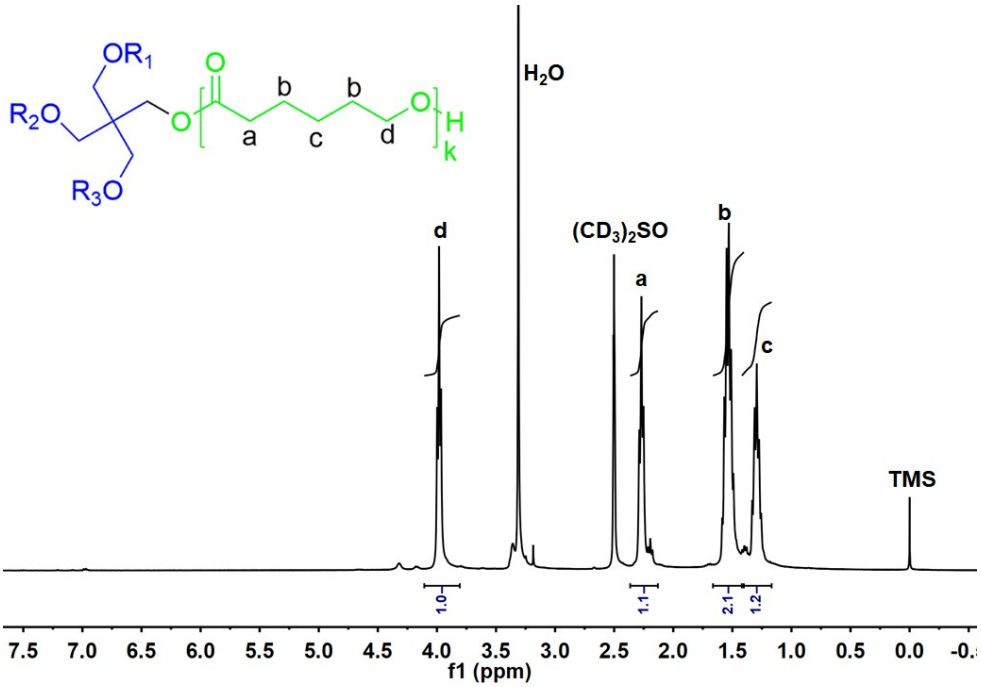


Fig. S3. [1]H NMR spectrum of SPCL in DMSO-d6.

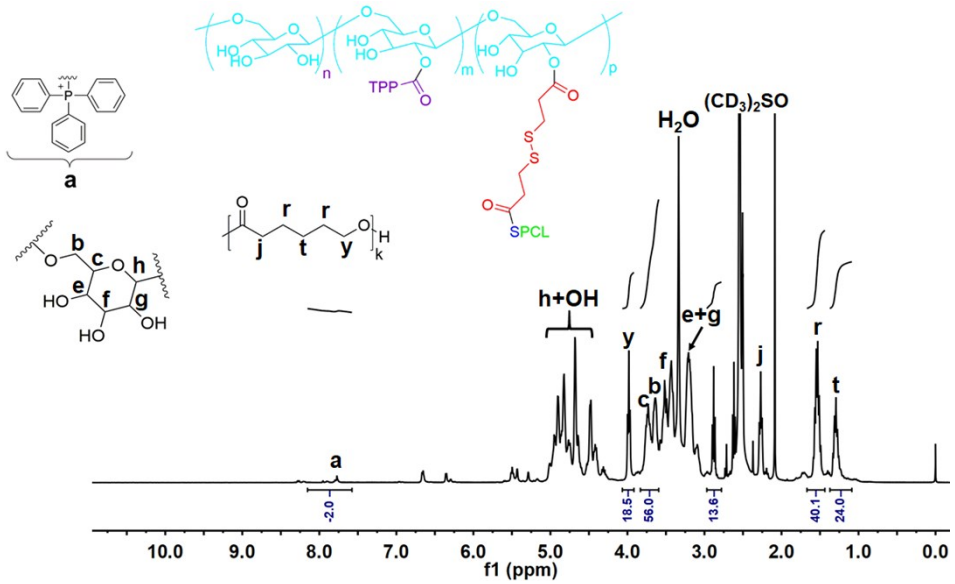
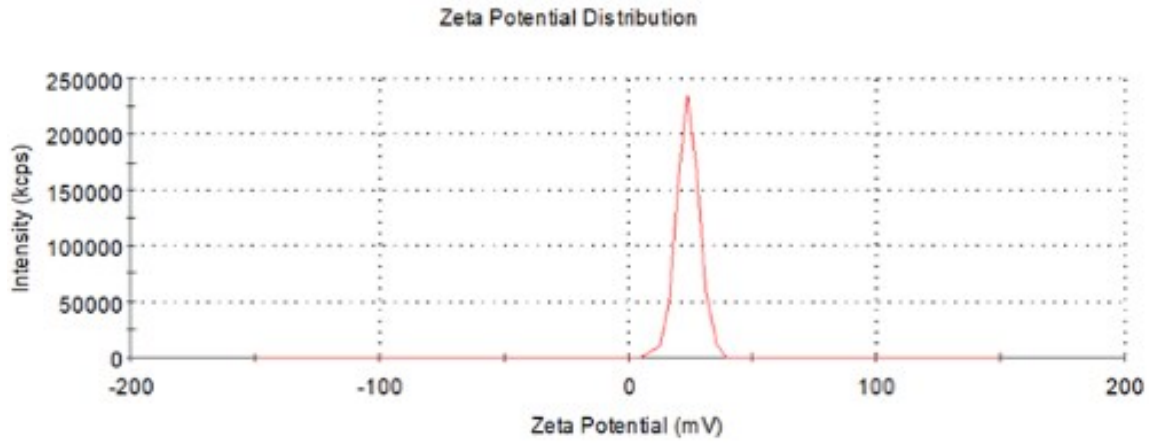


Fig. S4. [1]H NMR spectrum of TPP-Dex-ss-SPCL in DMSO-d6.



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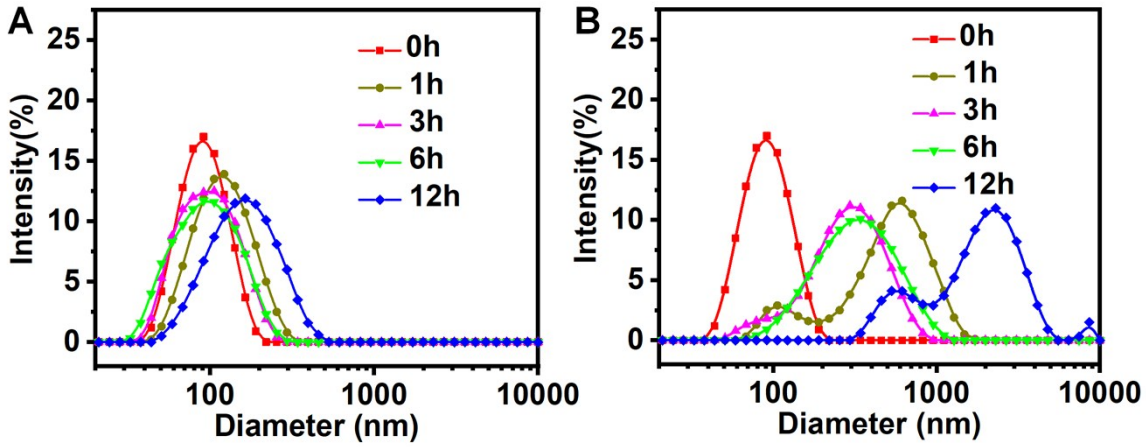

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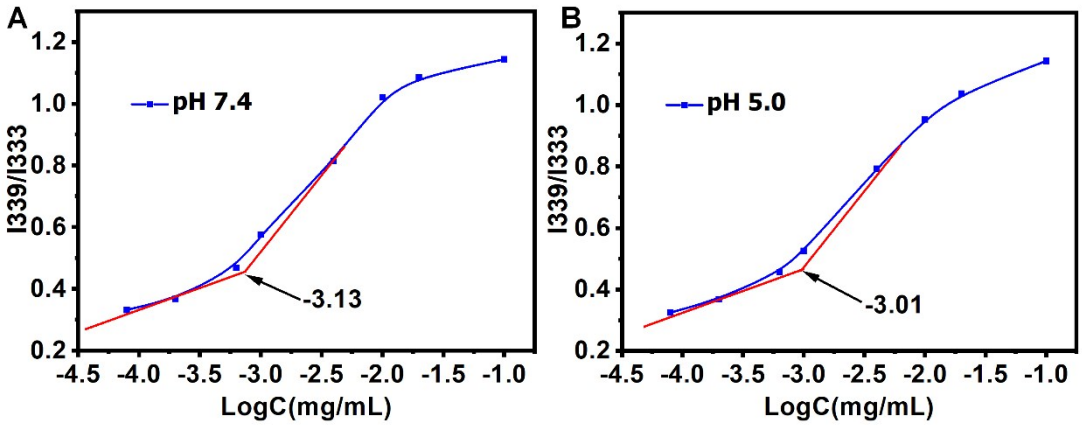
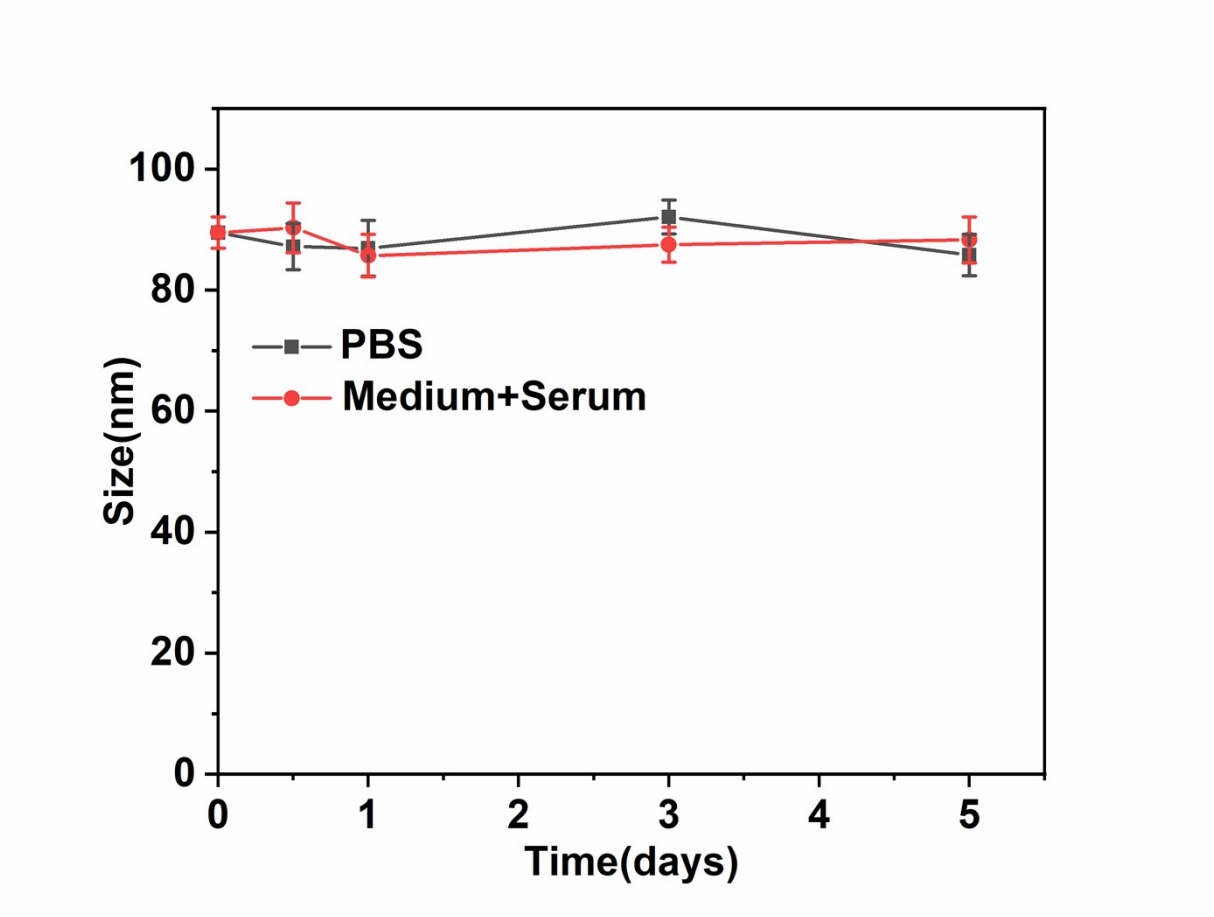


Fig. S7. The critical micelle concentration (CMC) of the TPP-Dex-ss-SPCL micelles at A) pH 7.5 or B) pH 5.0 condition derived from the plot of I339 /I333 ratio vs. copolymer concentration using pyrene as the probe.



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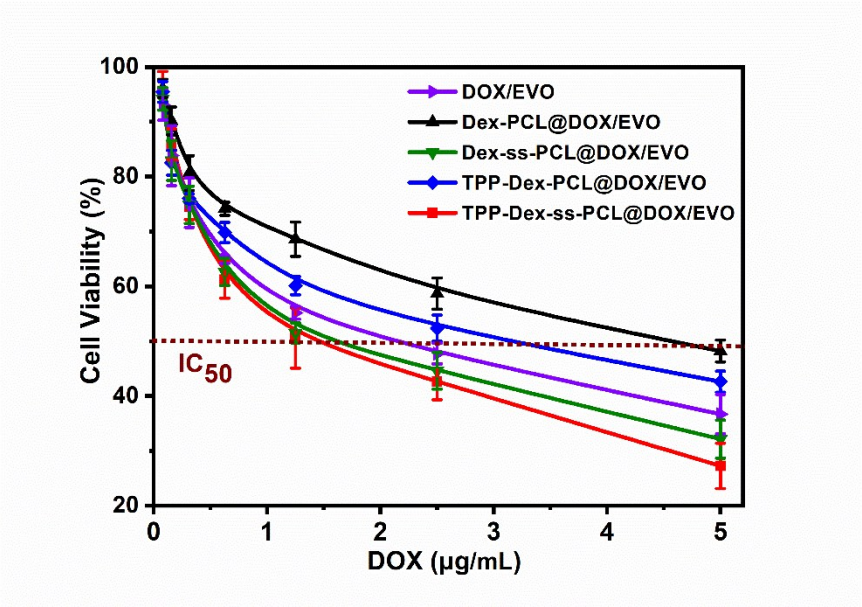

Fig. S9. Cytotoxicity of 4T1 cells treated by free drugs and drugs-loaded micelles as a function of DOX concentration (n = 3).

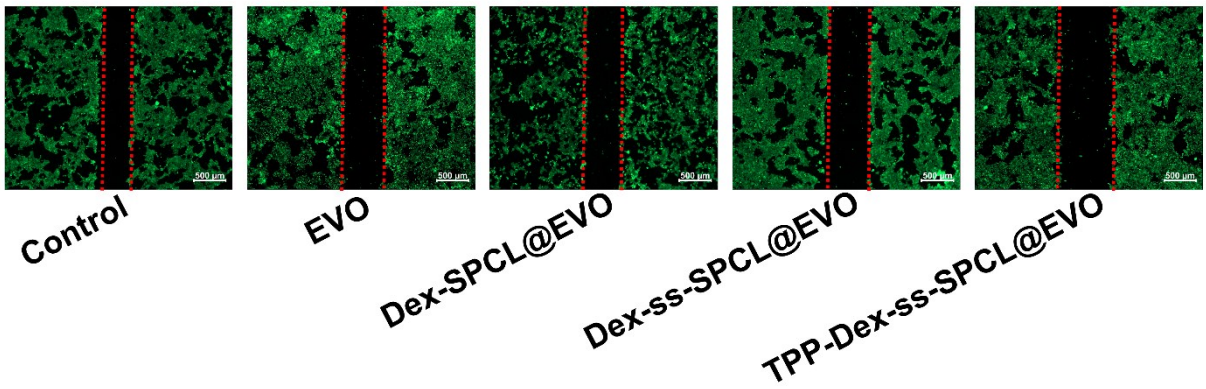

Fig. S10. Wound-healing assays showing that EVO inhibit the migration of 4T1 cells.

Table-S1

Sample name	Micelles size (nm)	PDI	Zeta potential(mV)	LC%	EE%
TPP-Dex-ss-SPCL	85.7±1.8	0.176±0.015	+22.7±0.4	—	—
Dex-ss-SPCL	96.5±3.6	0.143±0.022	-12.9±0.3	—	—
TPP-Dex-SPCL	88.6±2.5	0.194±0.035	+23.4±0.7	—	—
Dex-SPCL	82.9±4.6	0.158±0.014	-8.8±0.4	—	—
TPP-Dex-ss-SPCL@DOX/EVO	89.5±2.6	0.213±0.022	+24.4±0.5	6.81±0.25%[a] 5.64±0.16 %[b]	76.42±3.12%[a] 62.68±2.35%[b]
Dex-ss-SPCL@DOX/EVO	99.3±3.1	0.251±0.017	-9.6±0.6	7.26±0.37%[a] 6.63±0.15 %[b]	79.44±3.27%[a] 73.92±2.85%[b]
TPP-Dex-SPCL@DOX/EVO	91.2±4.5	0.226±0.025	+25.5±0.3	6.46±0.22%[a] 5.12±0.19 %[b]	72.04±3.35%[a] 56.97±2.82%[b]
Dex-SPCL@DOX/EVO	86.9±3.7	0.217±0.019	-6.4±0.8	7.34±0.27%[a] 6.46±0.18 %[b]	81.22±3.13%[a] 71.08±2.84%[b]

Micelles size, PDI and Zeta potential were all determined by DLS.
a stands for DOX, and b stands for EVO.