Supporting Information

Redox-sensitive Carrier-free Nanoparticles self-assembled by Disulfide-linked Paclitaxel-Tetramethylpyrazine Conjugate for Combination Cancer Chemotherapy

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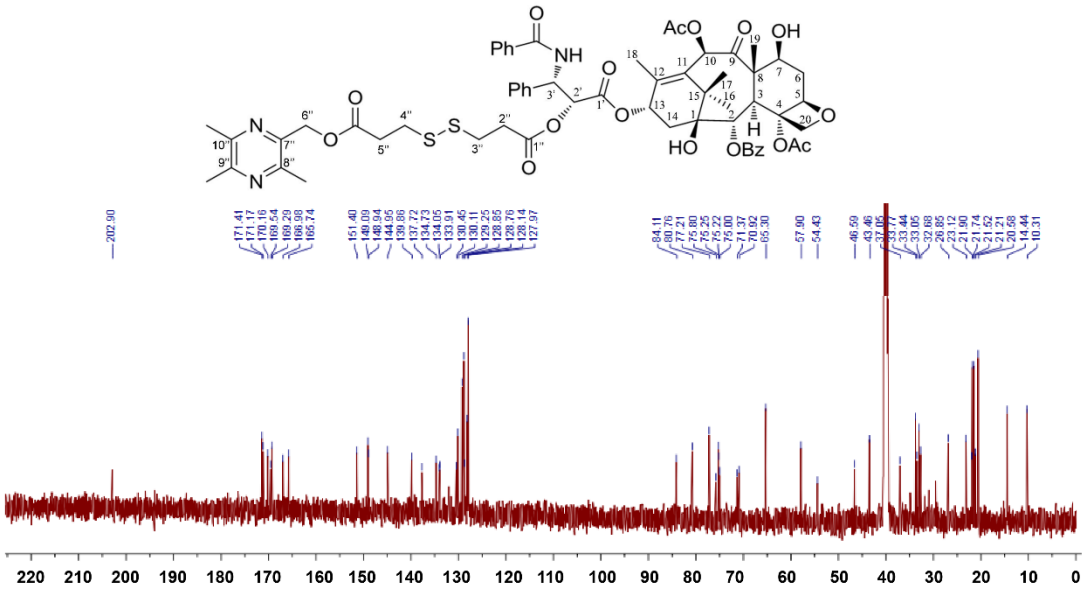

Figure S1. ^{13}C NMR spectrum of PTX-ss-TMP conjugate.

Table S1. ^{13}C NMR data of PTX-ss-TMP conjugate in DMSO-d_6 (150 MHz).

No.	δ (ppm)	No.	δ(ppm)	No.	δ(ppm)
1	77.2	15	43.3	6”	169.3
2	75.0	16	21.9	7”	151.4
3	46.6	17	26.9	8”	144.0
4	80.7	18	14.4	9”	148.9
5	84.1	19	10.31	10”	149.1
6	33.7	20	75.8	4-OAc	170.2, 23,2
7	70.9	1’	171.4	10-OAc	171.2, 21.7
8	57.9	2’	75.2	2-benzoyl	166.9, 130.1, 130.1, 127.9, 127.9, 133.9
9	202.9	3’	54.4	3’-N-benzoyl	169.5, 128.2, 128.2, 128.9, 128.9, 130.4
10	75.2	1”	165.7	3’-Ph	130.7, 127.9, 127.9, 129.3, 129.3, 128.8
11	134.0	2”	33.4	8”-Me	21.5
12	139.8	3”	65.3	9”-Me	20.6
13	71.4	4”	65.3	10”-Me	21.2
14	37.0	5”	33.1		

ESI spectrum of TMP-ss-PTX conjugate

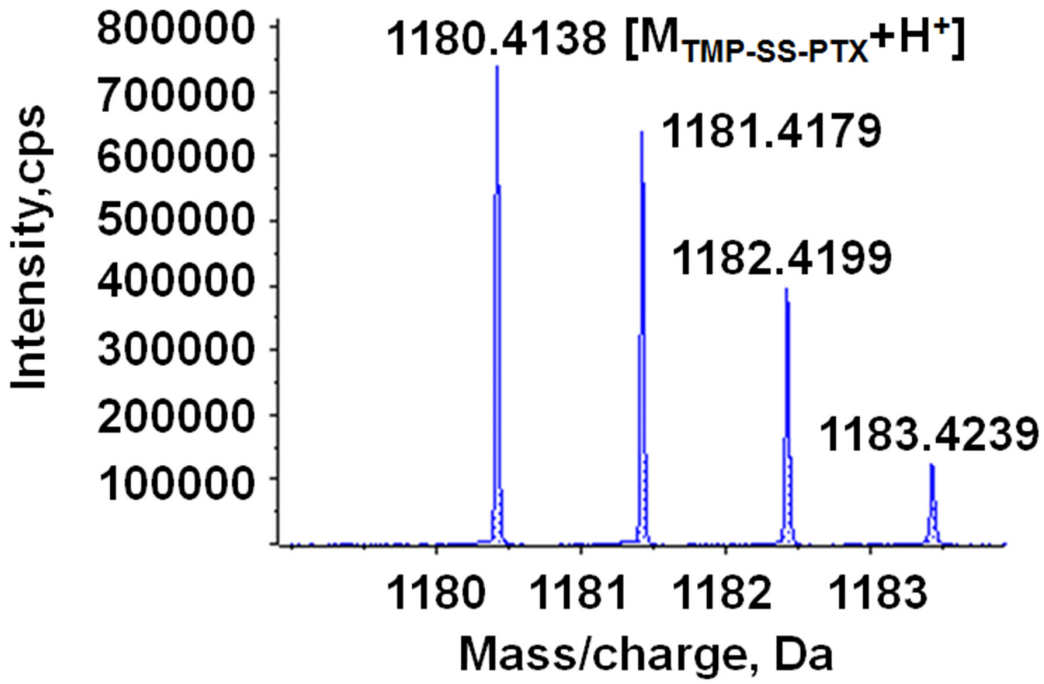

Figure S2. Q-TOF MS/MS spectrum of PTX-ss-TMP conjugate.

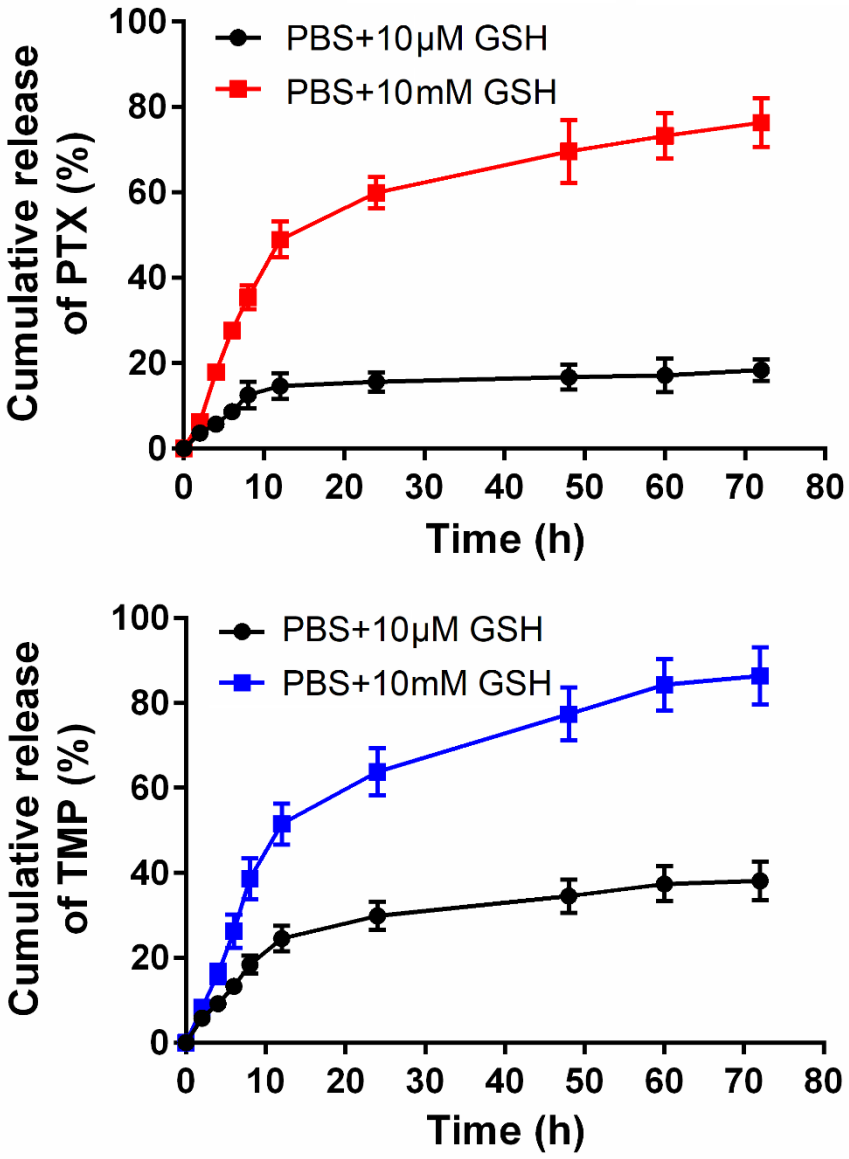

Figure S3. Redox-triggered drug release from the PTX-ss-TMP NPs at 37 °C in PBS with or without 10nM GSH (pH 7.4, n = 3).

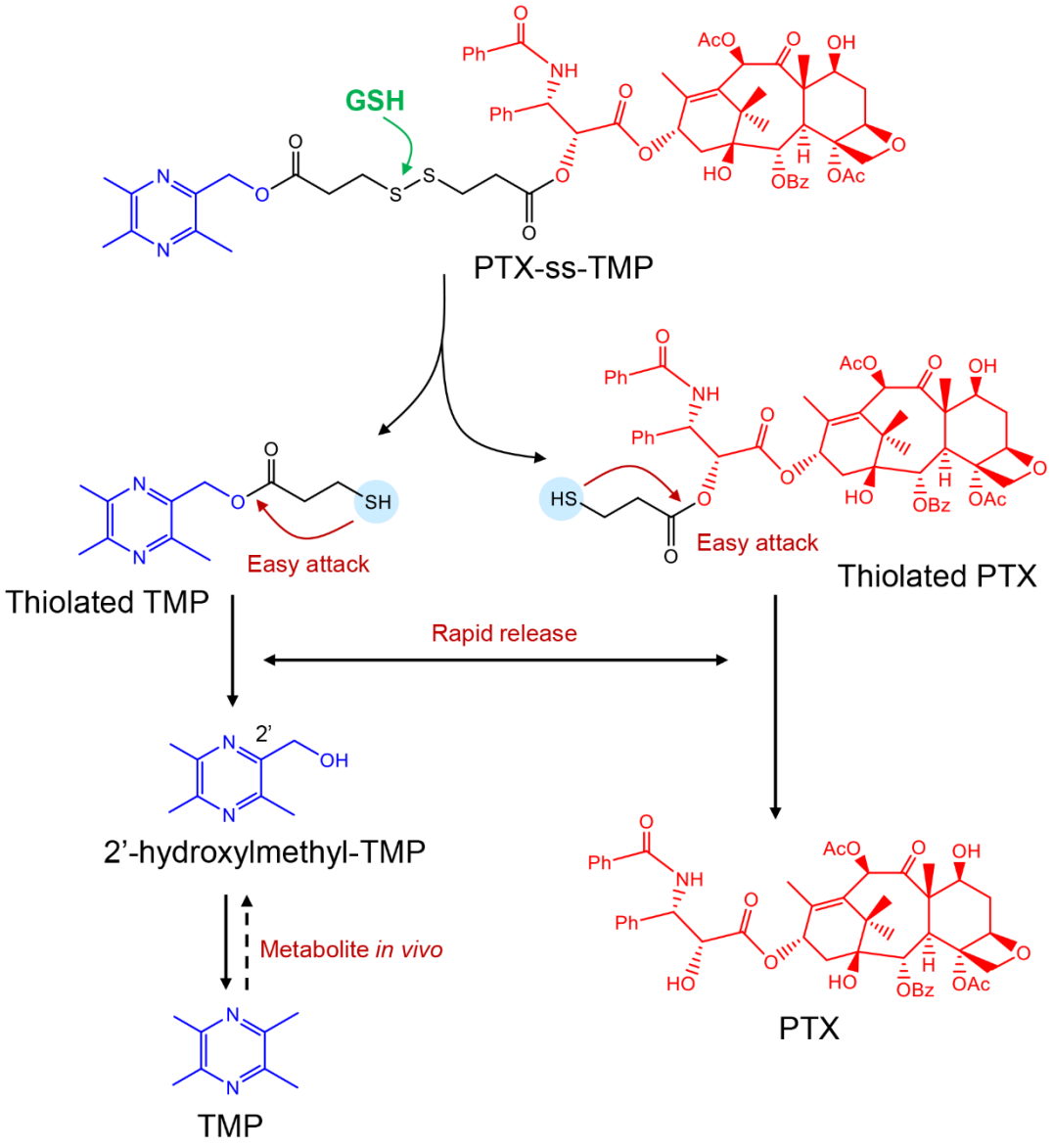

Figure S4. Mechanisms of the redox responsive drug release of disulfide bond triggered by GSH.

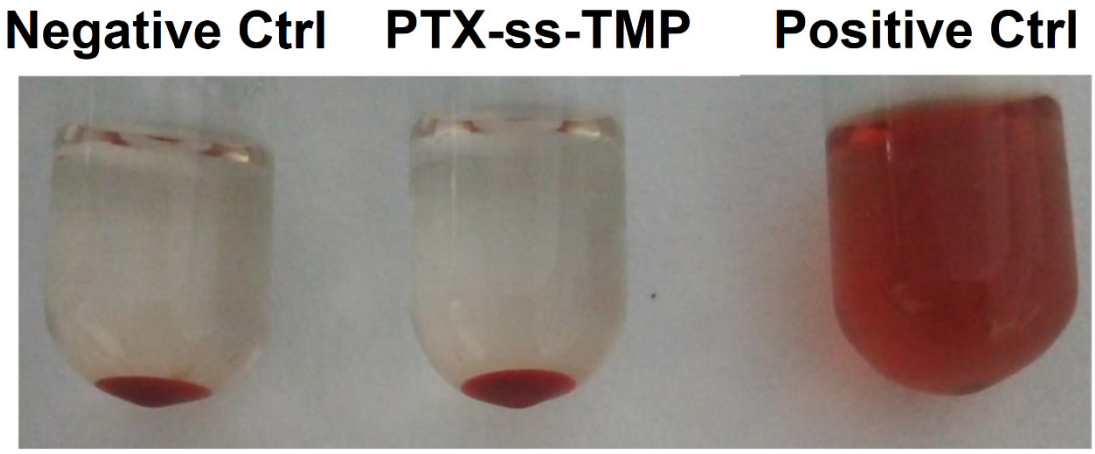

Figure S5. Hemolysis results of PTX-ss-TMP NPs after 24 h incubation.

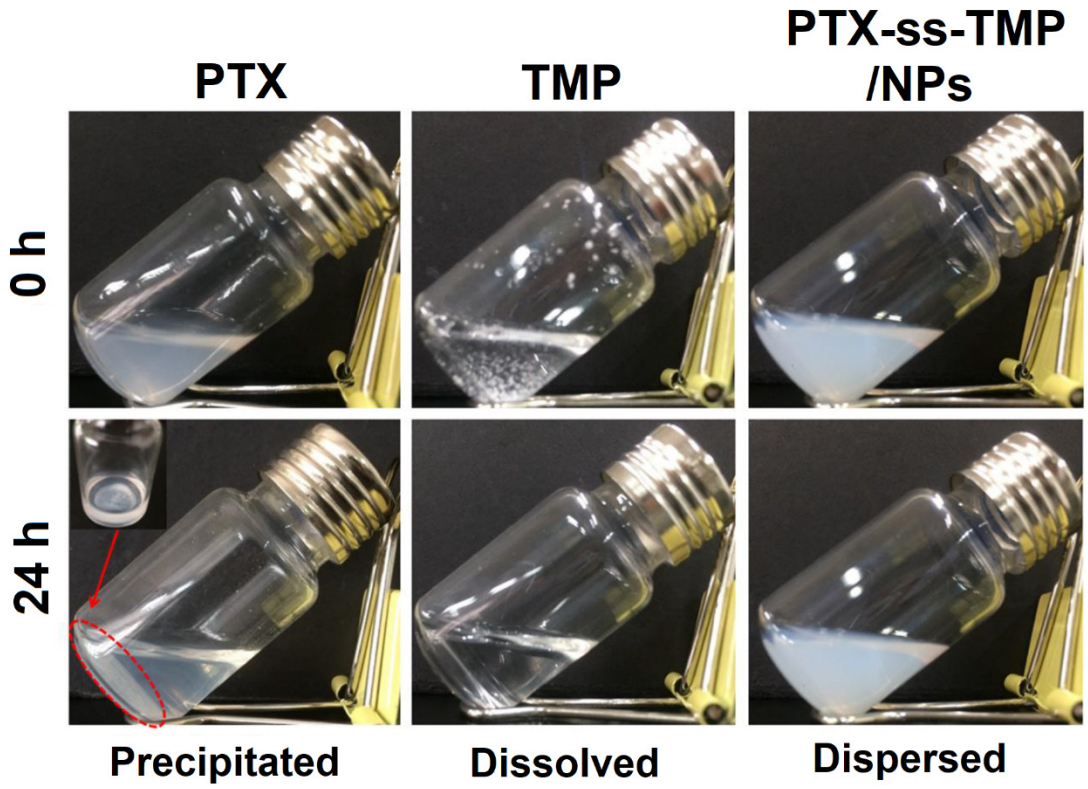

Figure S6. Photographs of free PTX (1 mg/mL) precipitated in PBS, free TMP (1 mg/mL) slightly dissolved in PBS, and PTX-ss-TMP NPs (2 mg/mL) dispersed in PBS.

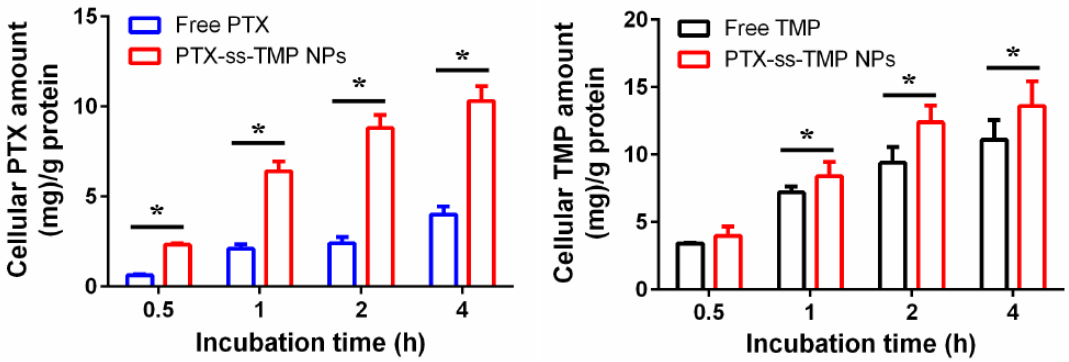

Figure S7. Intracellular uptake of PTX and TMP in A2780 cells after treatment with free PTX/TMP or PTX-ss-TMP NPs for 0.5, 1, 2, 4 h, respectively. PTX or TMP absorbed in cells was determined by HPLC method followed by a series of approaches descripted in Method Section.

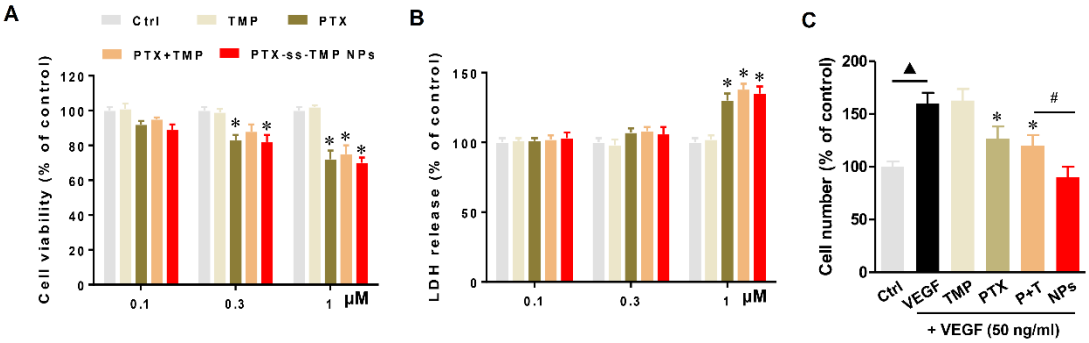

Figure S8. Effects of PTX-ss-TMP NPs on angiogenesis in vitro. (A) Effects of various formulas (free TMP, free PTX, PTX+TMP mixture, and PTX-ss-TMP NPs) at 0.1, 0.3, and 1 μM on HUVEC viability for 48h treatment. Cell viability was evaluated by MTT assays. (B) LDH release in HUVECs caused by various samples as above-mentioned. (C) Cell growth inhibition of various formulas at 0.1 μM based on VEGF stimulation.

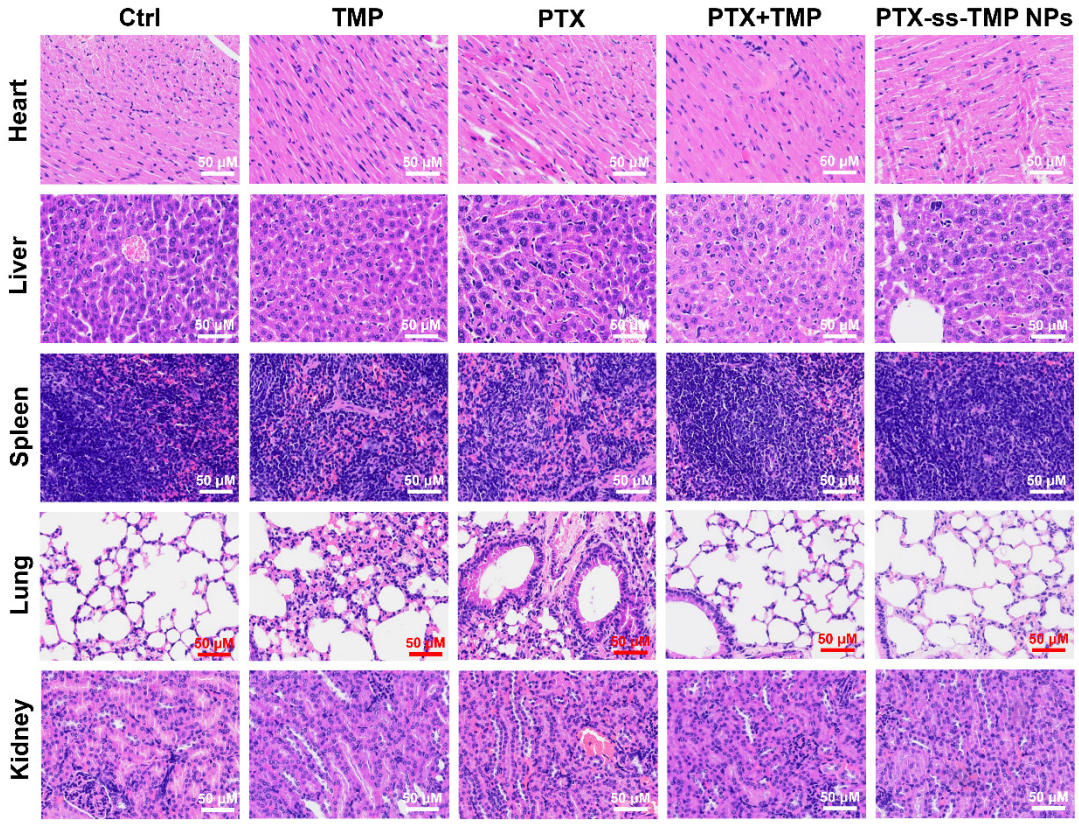

Figure S9. Histopathological analysis by hematoxylin and eosin (H&E) staining of heart, liver, spleen, lung, and kidney sections isolated from nude mice after treatment with saline, TMP, PTX, PTX and TMP mixture, and PTX-ss-TMP NPs, respectively.