Supporting information:

Reversibly pH-responsive and targeting nanocarriers based on poly (tannic acid) and HER2 antibody modified mesoporous silica nanoparticles for targeted tumor therapy

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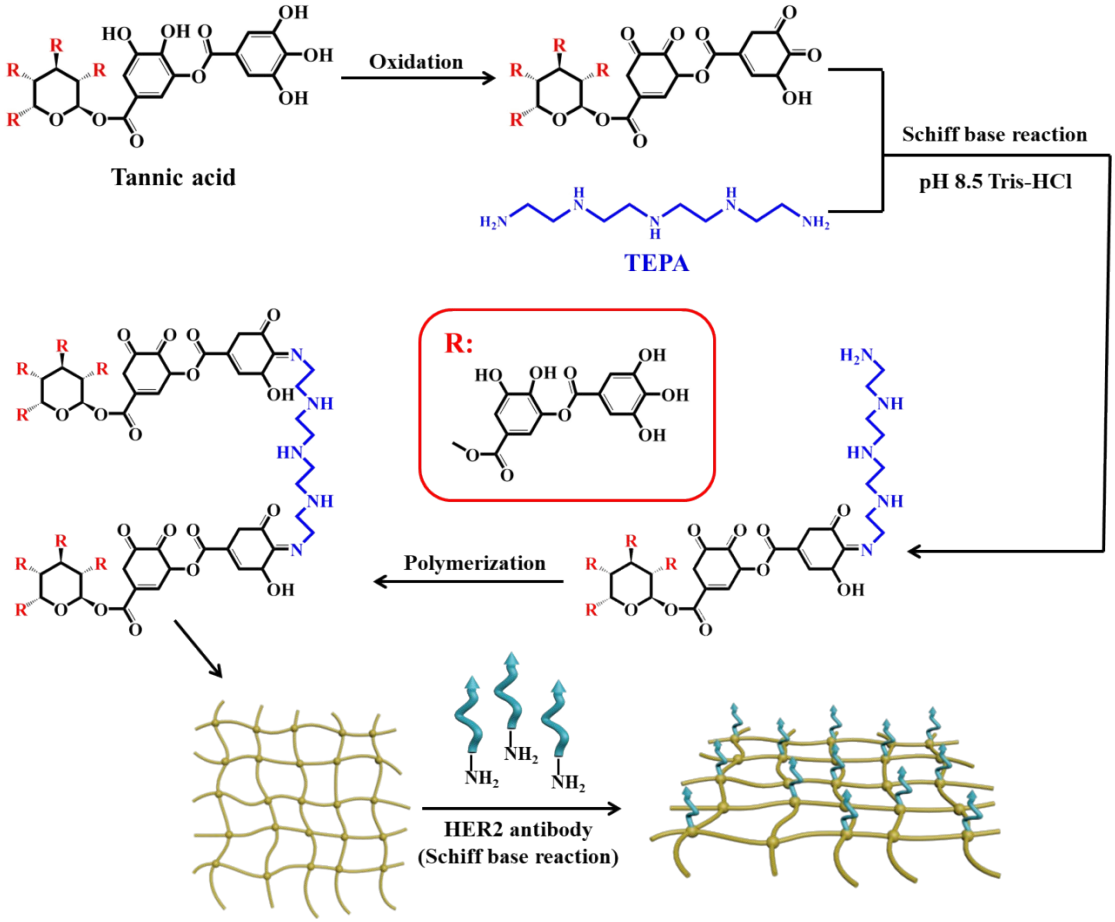
Cell culture:

Human breast carcinoma cell line (SK-BR-3) and human normal hepatic cell line (L-02) were obtained from the Cell Bank of Chinese Academy of Sciences (Shanghai, China). Dulbecco's modified eagle's medium (DMEM), trypsin and fetal bovine serum (FBS) were purchased from Thermo Fisher Scientific- CN.

L-02 and SK-BR-3 were cultured in DMEM medium containing 10% fetal bovine serum, 100 μg/mL streptomycin, and 100 U/mL penicillin. The above cells were cultured in 5% CO_2 incubator at 37 °C. The medium was changed every two days, and the adherent cells were trypsinzed every four days.



Scheme S1. Possible reaction mechanism for the formation of PTA and the covalent graft of HER2 antibody.

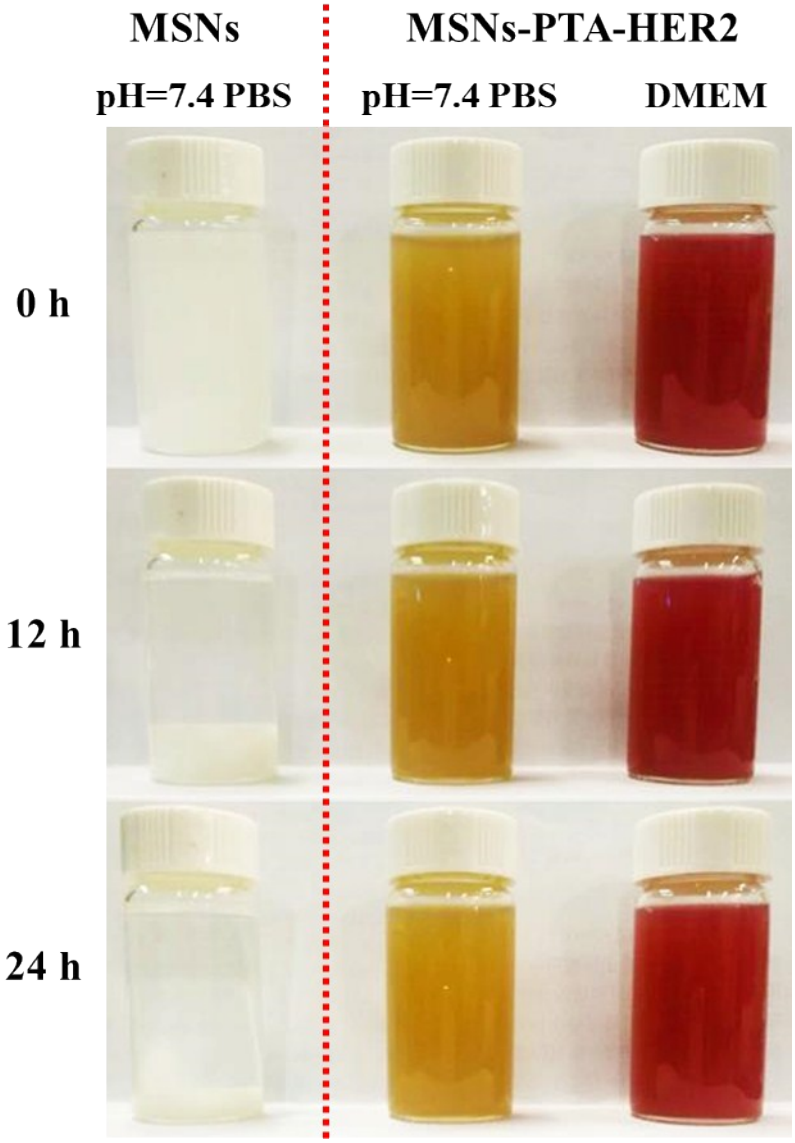


Figure S1. Photographs of MSNs and MSNs-PTA-HER2 dispersed in different medium with a concentration of 4 mg/mL. All these photographs are taken at different periods after dispersion by sonication.

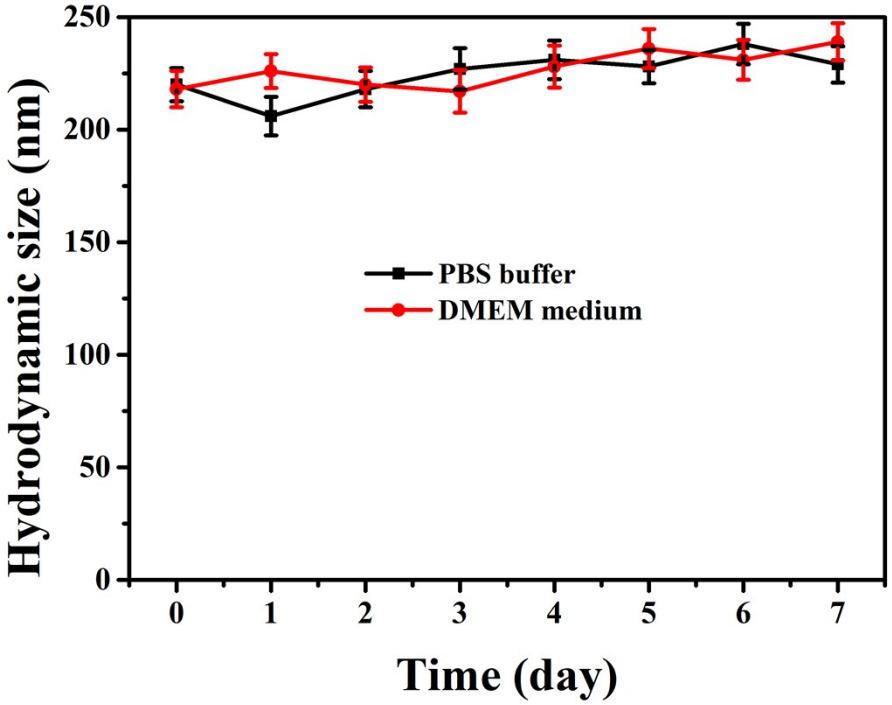


Figure S2. Long-term colloidal stability of MSNs-PTA-HER2 in the presence of PBS buffer (pH 7.4) and culture media (DMEM+10% FBS) measured by dynamic light scattering (DLS). Data are represented as mean ± SD (n = 3).

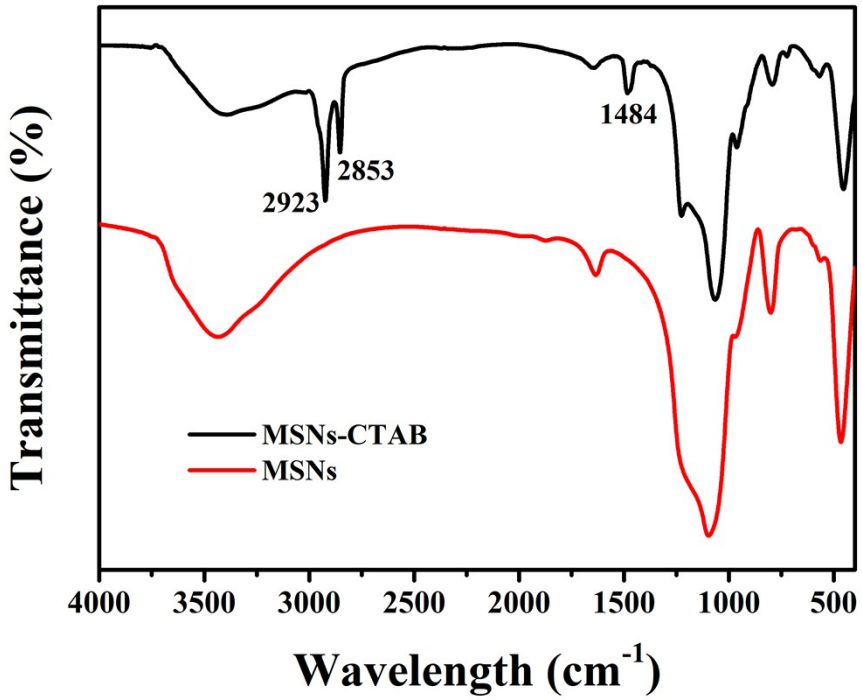


Fig. S3. FTIR spectra of CTAB-MSNs and MSNs.

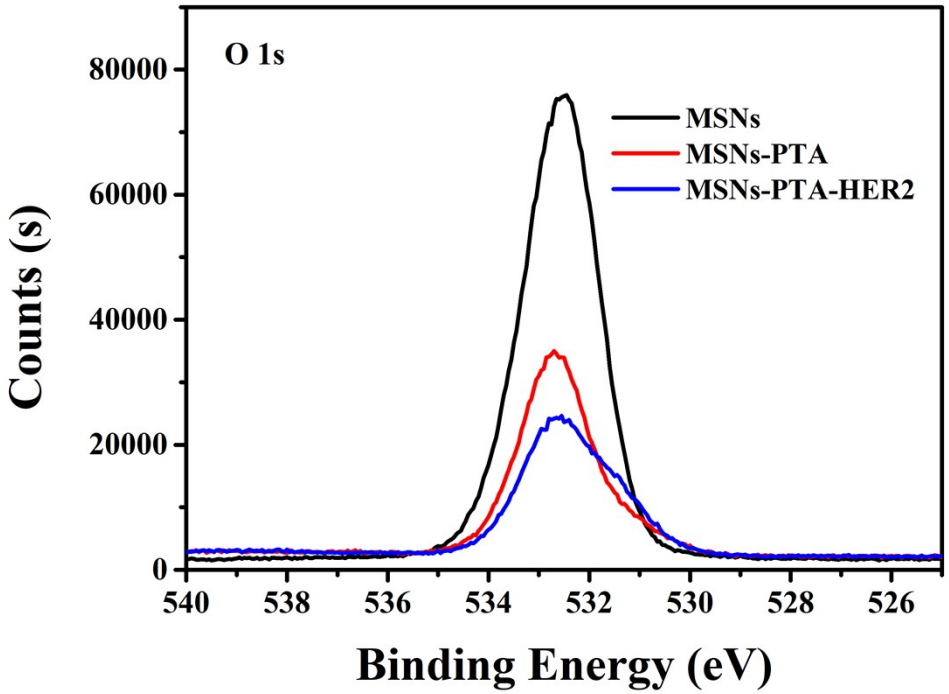


Fig. S4. Narrow scan XPS O 1s spectra of MSNs, MSNs-PTA and MSNs-PTA-HER2.

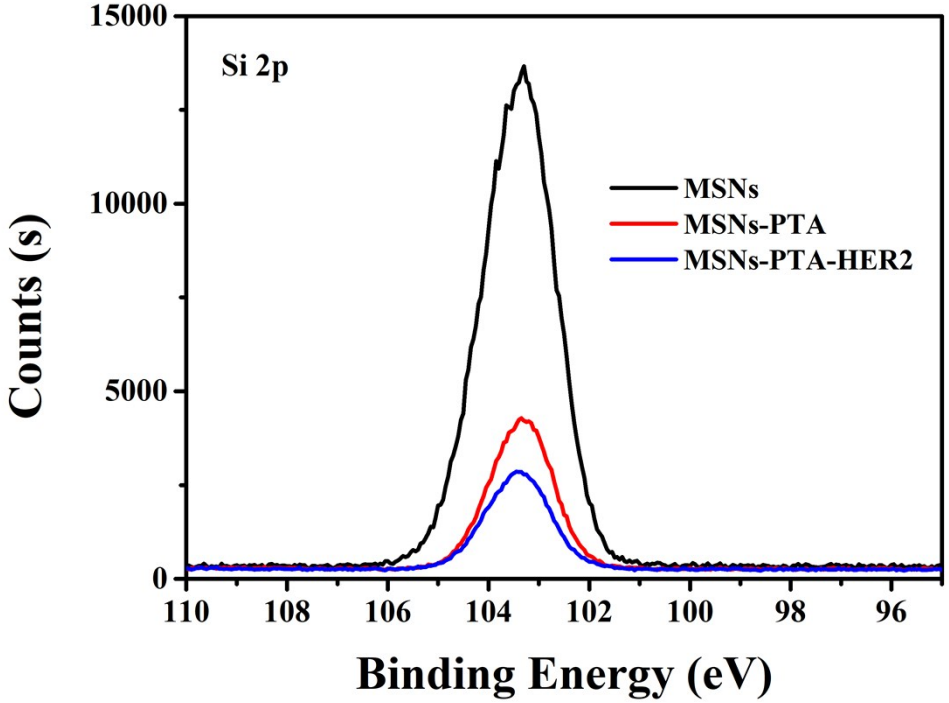


Fig. S5. Narrow scan XPS Si 2p spectra of MSNs, MSNs-PTA and MSNs-PTA-

HER2.

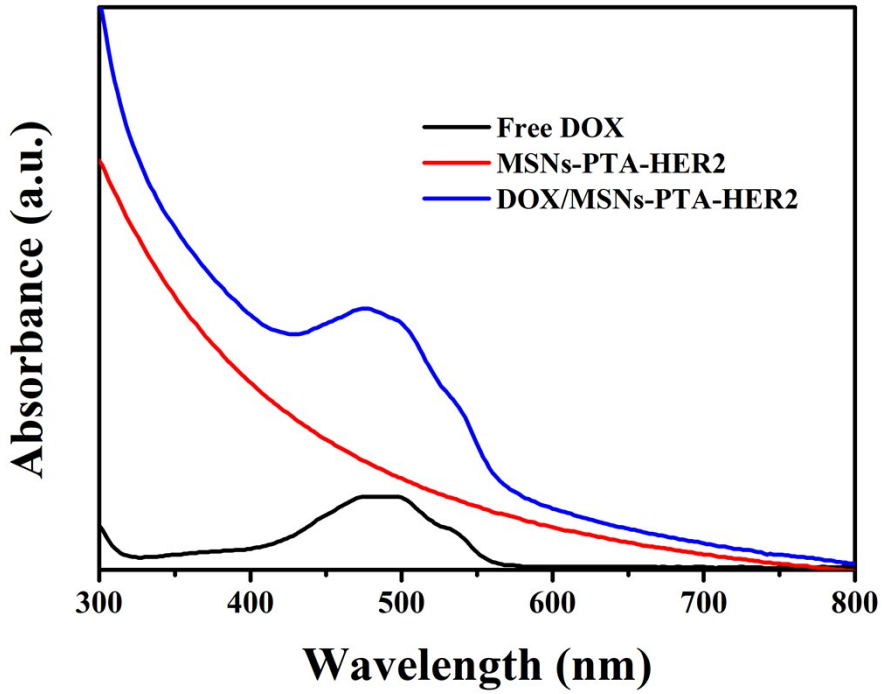


Fig. S6. UV-vis absorption spectra of free DOX, MSNs-PTA-HER2 and DOX/MSNs-PTA-HER2.

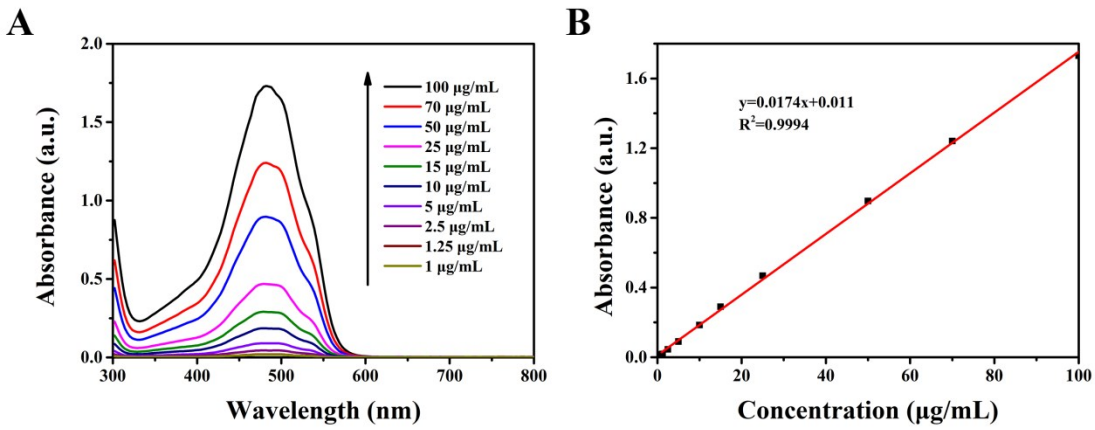


Fig. S7. (A) UV-vis absorption spectra of DOX with different concentrations; (B) DOX standard curve with absorption measured at 485 nm.

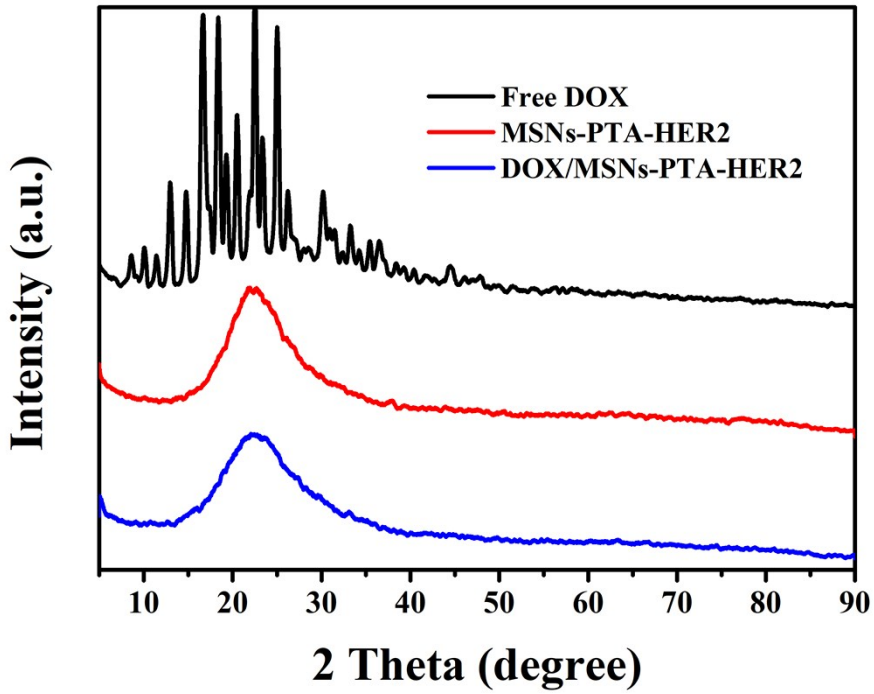


Fig. S8. Wide-angle XRD spectra of free DOX, MSNs-PTA-HER2 and DOX/MSNs-PTA-HER2.

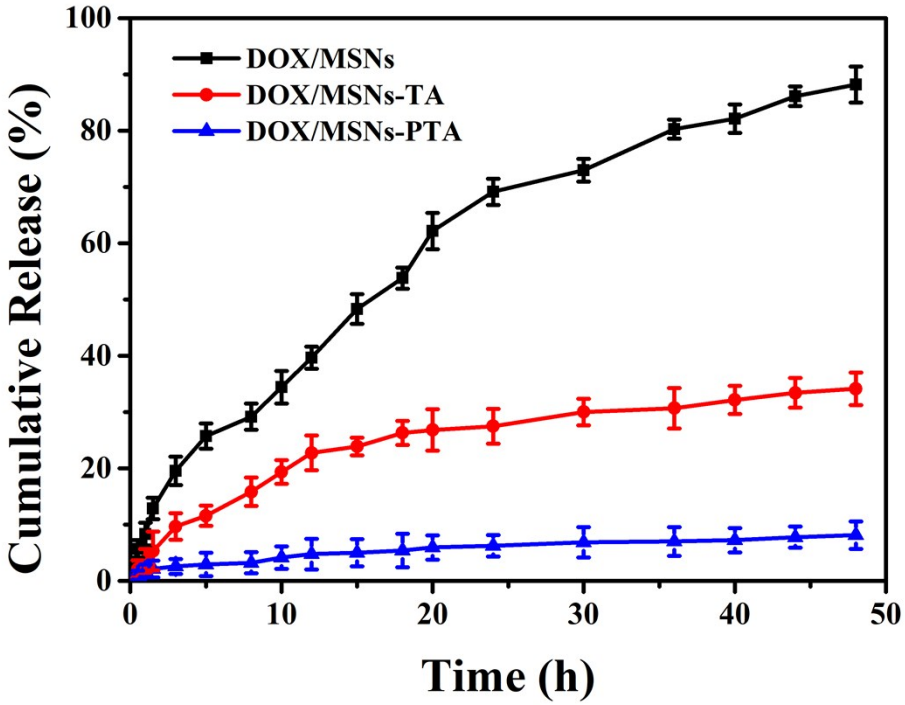


Fig. S9. The release profile of DOX from DOX/MSNs, DOX/MSNs-TA and DOX/MSNs-PTA at pH 7.4, respectively. Data are represented as mean ± SD (n = 3).

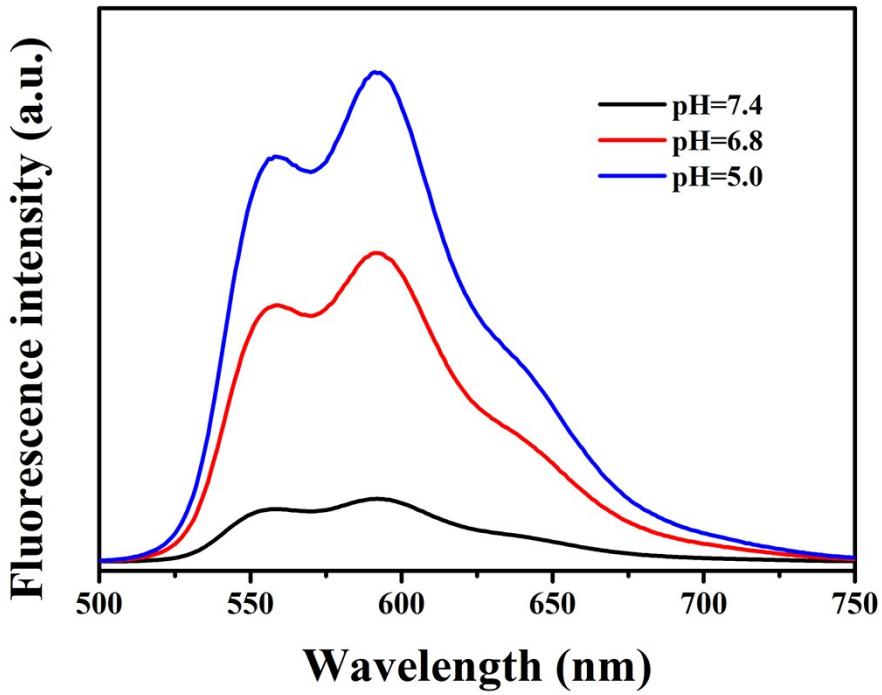


Fig. S10. Fluorescence spectra of released DOX (λ_{ex}= 485 nm) from DOX/MSNs-PTA-HER2 under different pH conditions (pH 7.4, 6.8 and 5.0).

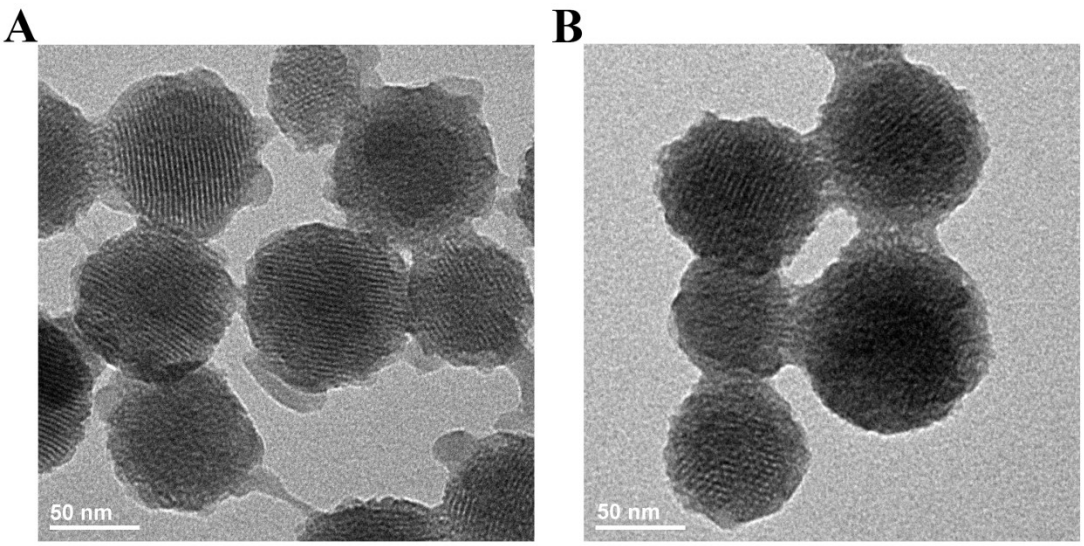


Fig. S11. (A) TEM image of MSNs-PTA treated at pH 5.0 for 24 h. (B) TEM image of MSNs-PTA treated at pH 5.0 for 24 h and pH 7.4 for another 24 h.

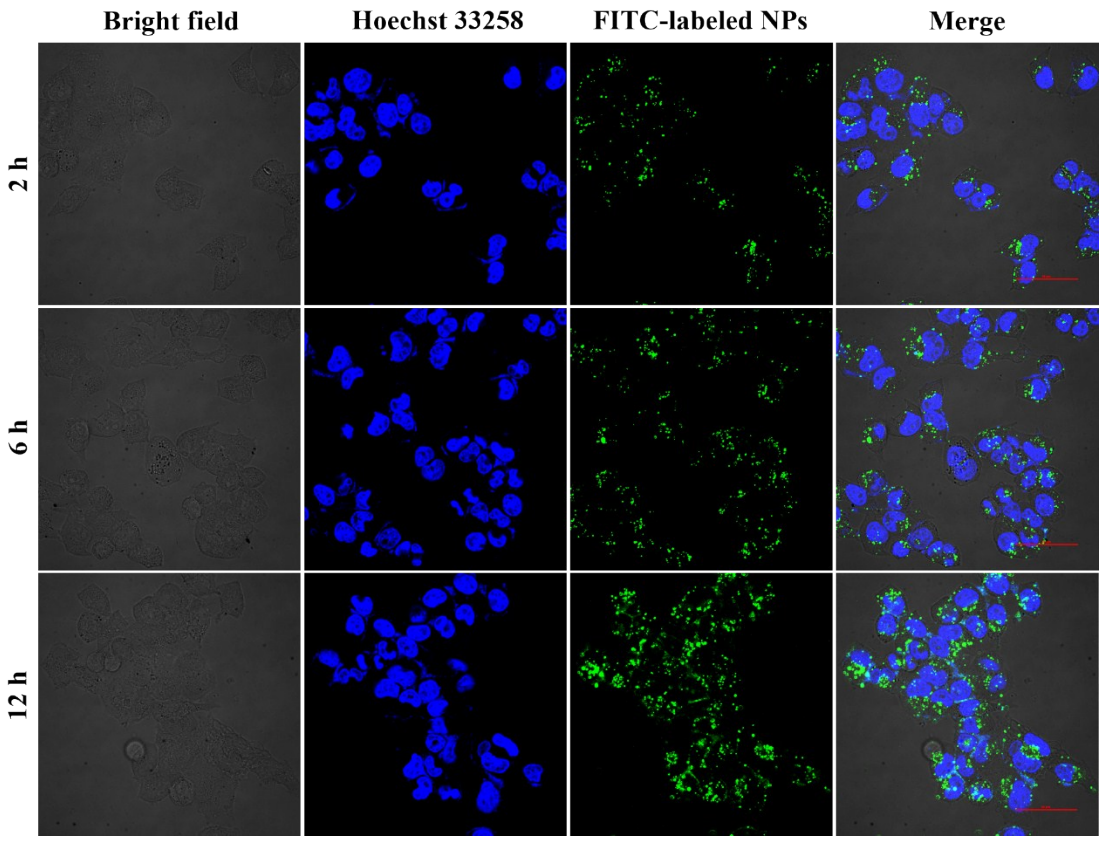


Fig. S12. CLSM images of SK-BR-3 cells incubated with FITC labeled MSNs-PTA-HER2 for 2 h, 6 h and 12 h, respectively. FITC labeled nanoparticles are seen in green channel, and Hoechst 33258 stained nucleus is seen in blue channel. Scale bar: 50 μm.

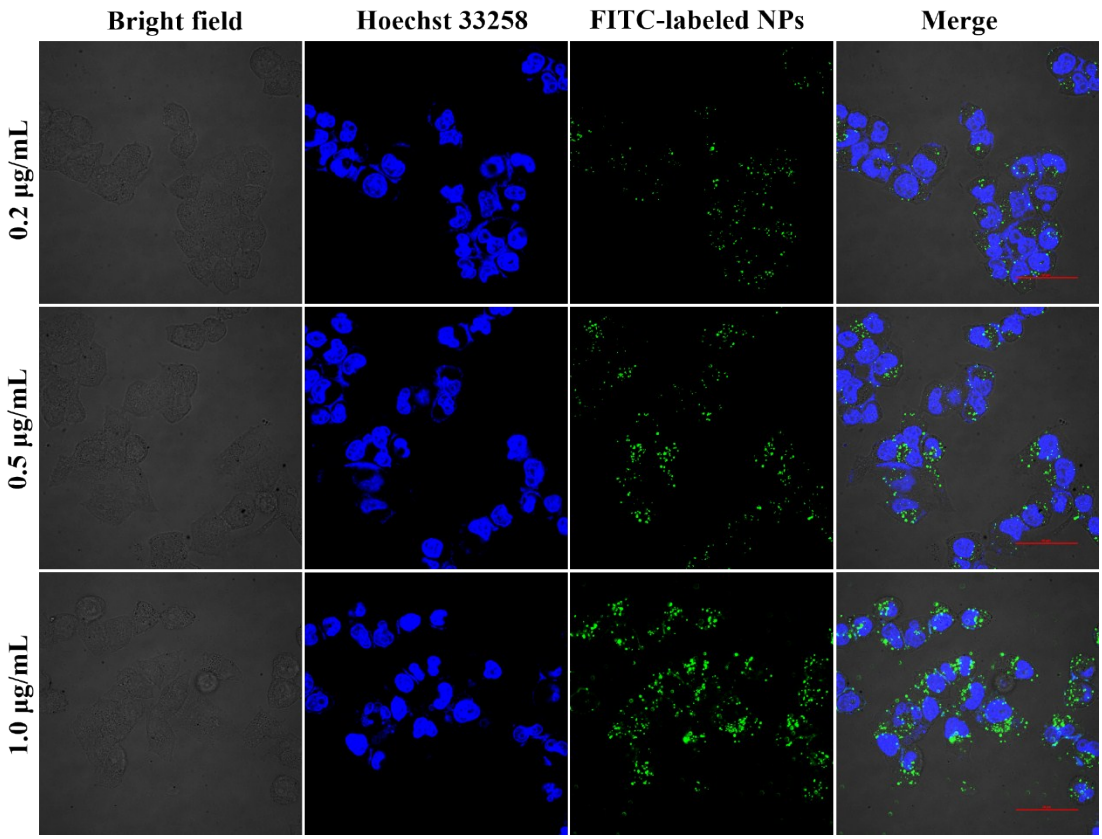


Fig. S13. CLSM images of SK-BR-3 cells incubated with different concentrations of FITC labeled MSNs-PTA-HER2 for 12 h, respectively. FITC labeled nanoparticles are seen in green channel, and Hoechst 33258 stained nucleus is seen in blue channel. Scale bar: 50 μm.

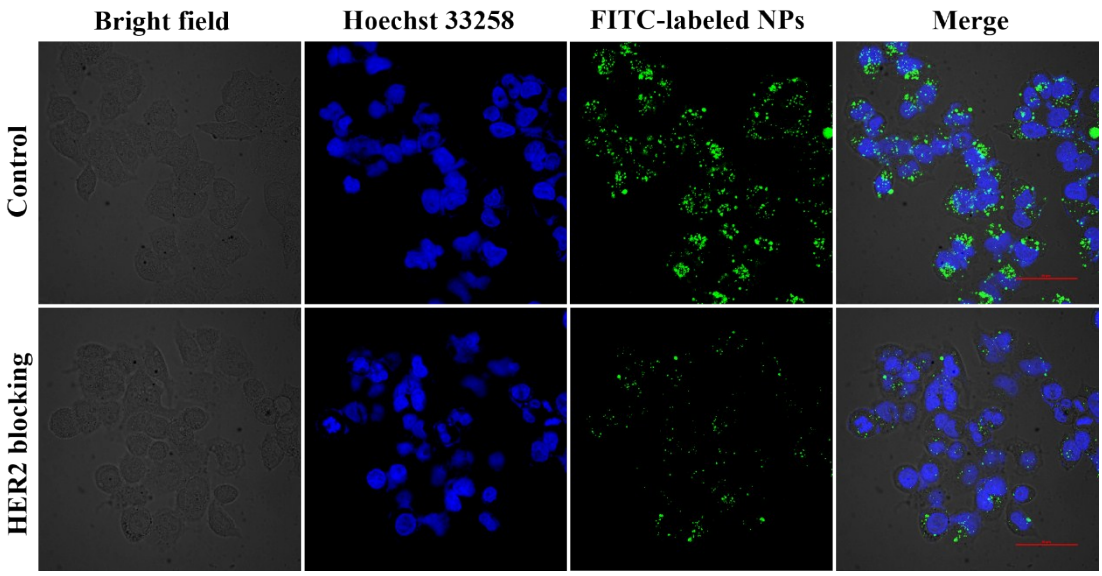


Fig. S14. CLSM images of SK-BR-3 cells pretreated with excessive free HER2 antibody (100 μg/mL), followed by incubation with MSNs-PTA-HER2 for another 12 h. Scale bar: 50 μm.

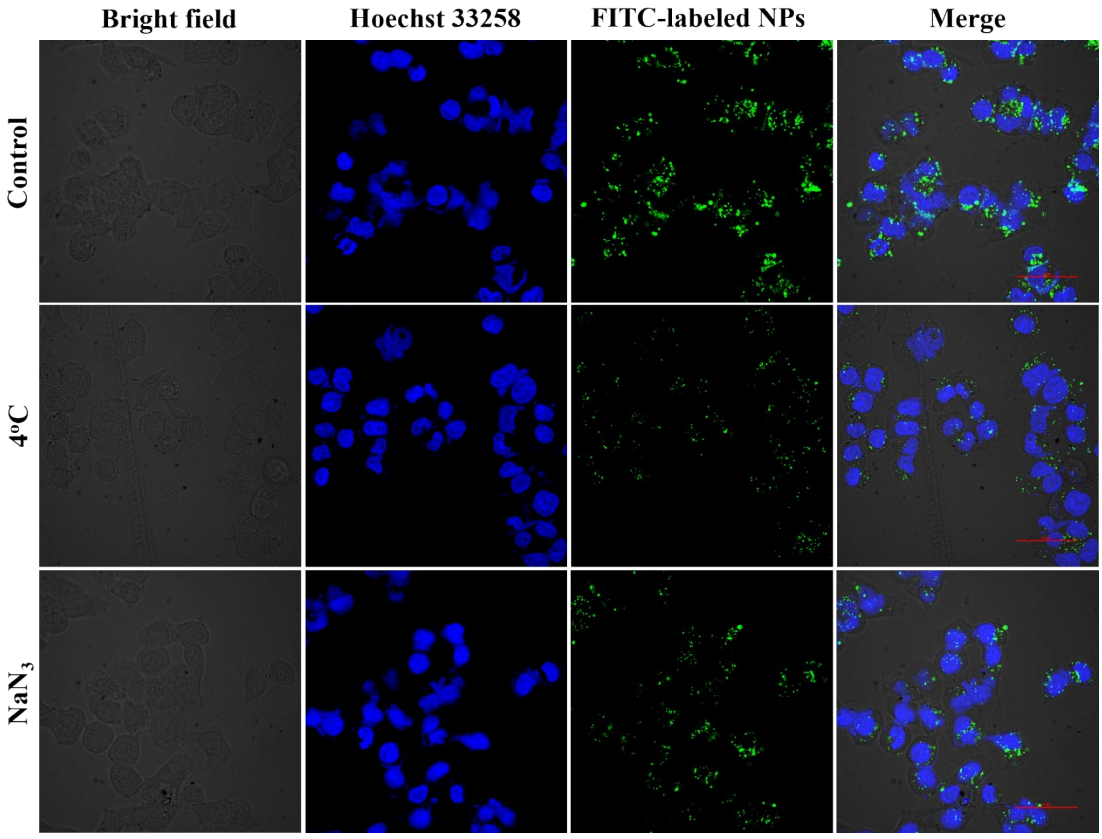


Fig. S15. CLSM image of SK-BR-3 cells incubated with MSNs-PTA-HER2 for 12 h at 4°C. And CLSM images of SK-BR-3 cells pretreated with NaN_3 for 2 h, followed by incubation with MSNs-PTA-HER2 for another 12 h. Scale bar: 50 μm.

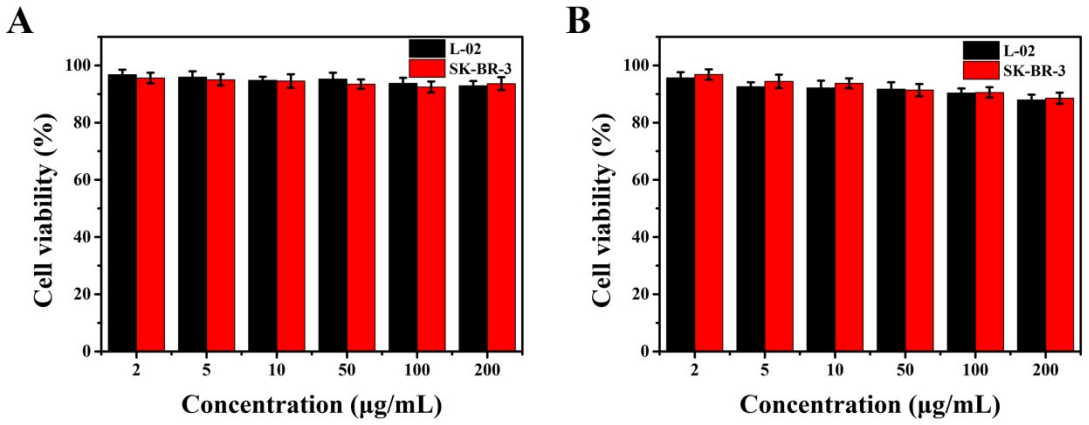


Fig. S16. *In vitro* biocompatibility analysis. Cell viability of L-02 and SK-BR-3 after (A) 24 h and (B) 48 h incubation with different concentrations of MSNs-PTA-HER2.

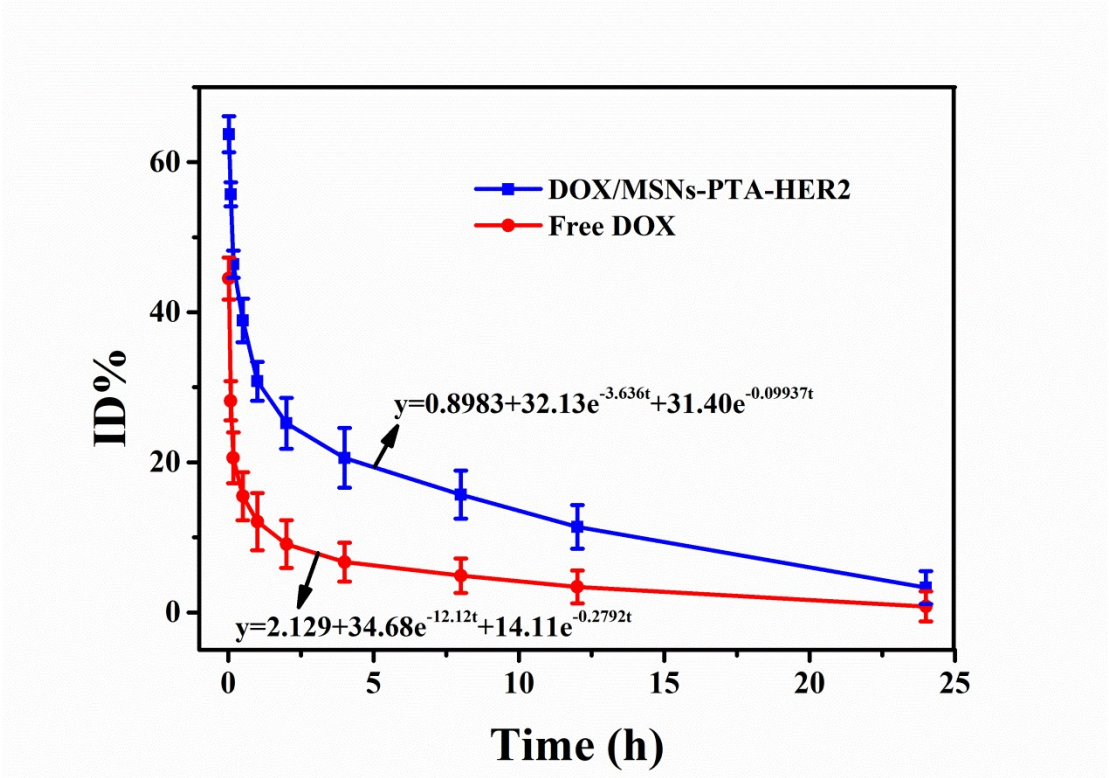


Fig. S17. Blood clearance curves of free DOX and DOX/MSNs-PTA-HER2 in mice.

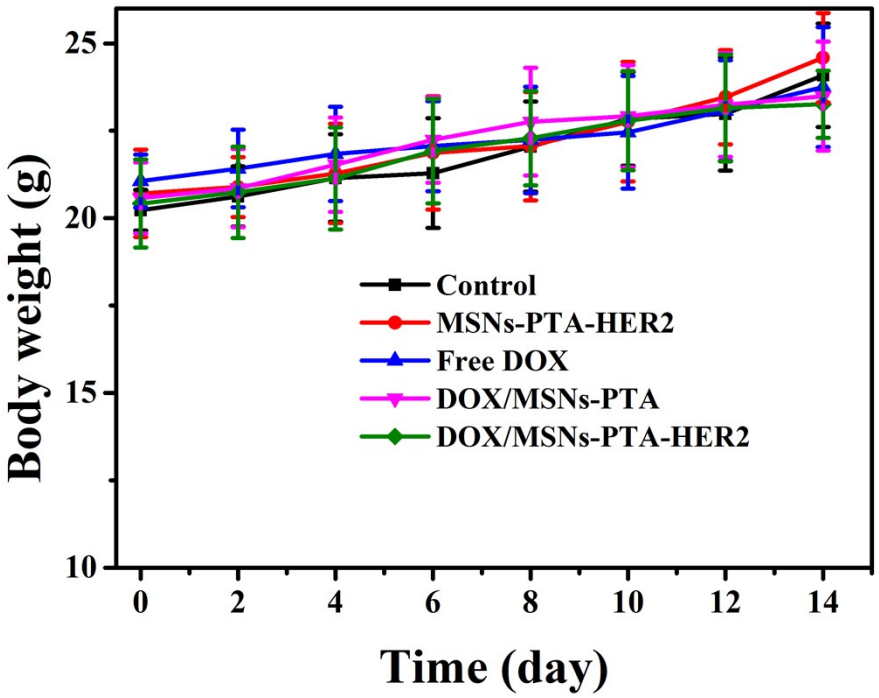


Fig. S18. Average body weight of mice of each group in different days.

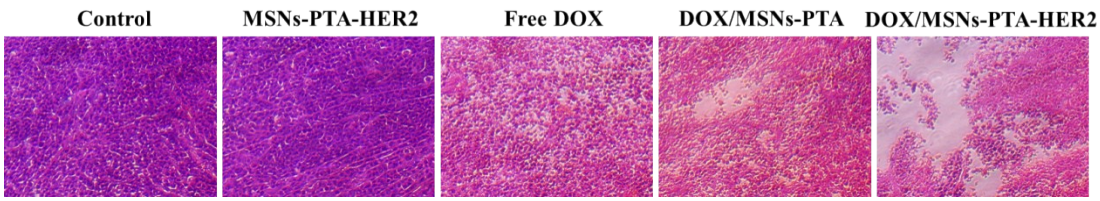


Fig. S19. Standard H&E staining of sliced typical tumor tissue of each group after treatment for two weeks.

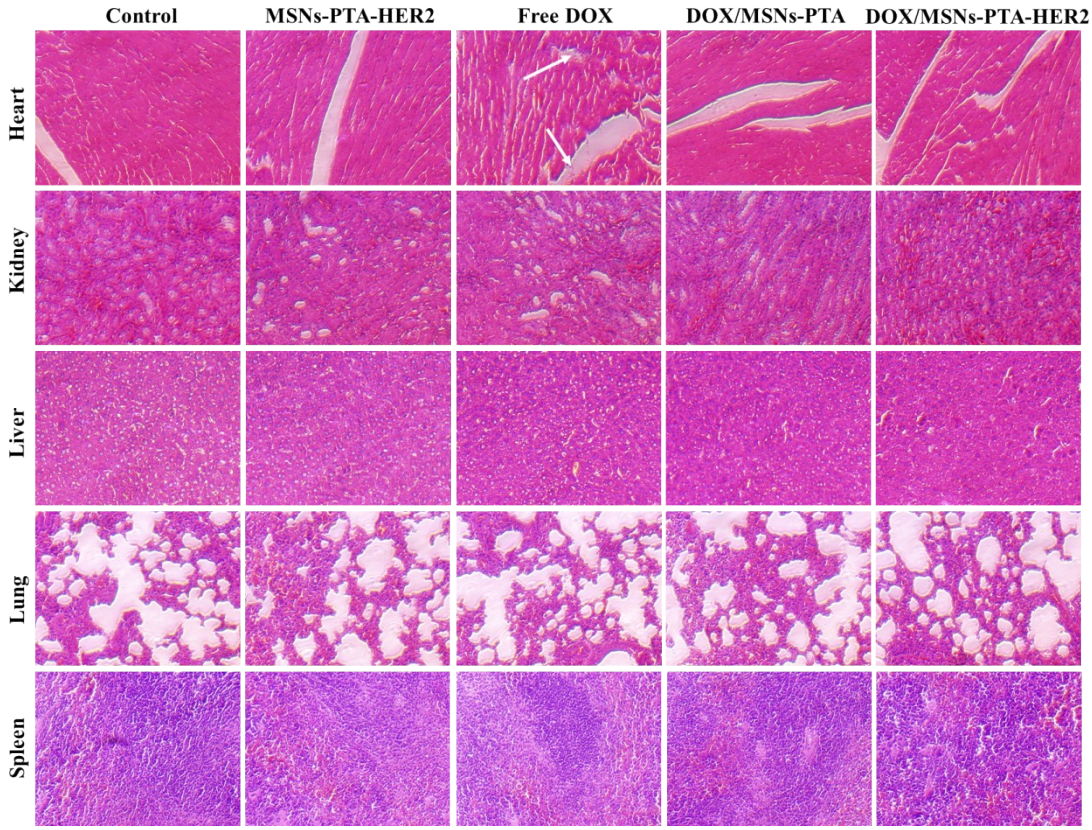


Fig. S20. Standard H&E stained images of typical heart, kidney, liver, lung and spleen tissues for control, MSNs-PTA-HER2, free DOX, DOX/MSNs-PTA and DOX/MSNs-PTA-HER2 groups after treatment for 14 days.

Table S1. The hydrodynamic size distribution in water.

Sample	Size (nm)	PDI
MSNs	122 ± 3.2	0.164
MSNs-PTA	190 ± 4.3	0.197
MSNs-PTA-HER2	220 ± 2.7	0.205

Table S2. Zeta potential results of MSNs before and after grafting with chemicals at each step.

Materials	Zeta Potential (mV)
MSNs	-26.2 ± 1.2
MSNs-PTA	-6.7 ± 0.5
MSNs-PTA-HER2	-13.6 ± 1.0

Table S3. The surface functionalization extent of MSNs was characterized by TGA analysis and the final weight losses for all materials are presented as follow.

Materials	Final weight loss (wt %)
MSNs	7.63
MSNs-TA	10.82
MSNs-PTA	31.60
MSNs-PTA-HER2	42.95

Table S4. The N_2 adsorption-desorption parameters of different functionalized MSNs.

Sample	S_{BET}(m^2/g)	V_P（cm^3/g）	W_{BJH}（nm）
MSNs	932.34	0.652	2.73
MSNs-PTA	573.43	0.446	2.21
MSNs-PTA-HER2	312.45	0.342	2.02

Table S5. Element components for the synthesized MSNs, MSNs-PTA and MSNs-PTA-HER2.

Sample	Element (at. %)			
	C	N	O	Si
MSNs	--	--	64.95	34.03
MSNs-PTA	43.59	9.42	35.52	11.47
MSNs-PTA-HER2	49.42	11.29	30.30	8.12

Table S6. IC_{50} value for different DOX loaded samples and free DOX for inhibiting growth of SK-BR-3 cells and L-02 cells after 24 h incubation.

Formulations	IC_{50} (μg/ml)	
	SK-BR-3 cells	L-02 cells
Free DOX	0.42	0.47
DOX/MSNs-PTA	0.76	0.82
DOX/MSNs-PTA-HER2	0.32	1.19

Abbreviations: IC_{50}, half maximal inhibitory concentration, the drug concentration at which the growth of 50% cells was inhibited.