Supplementary information

Transforming growth factor-β blockade modulates tumor mechanical microenvironment for enhanced antitumor efficacy of photodynamic therapy

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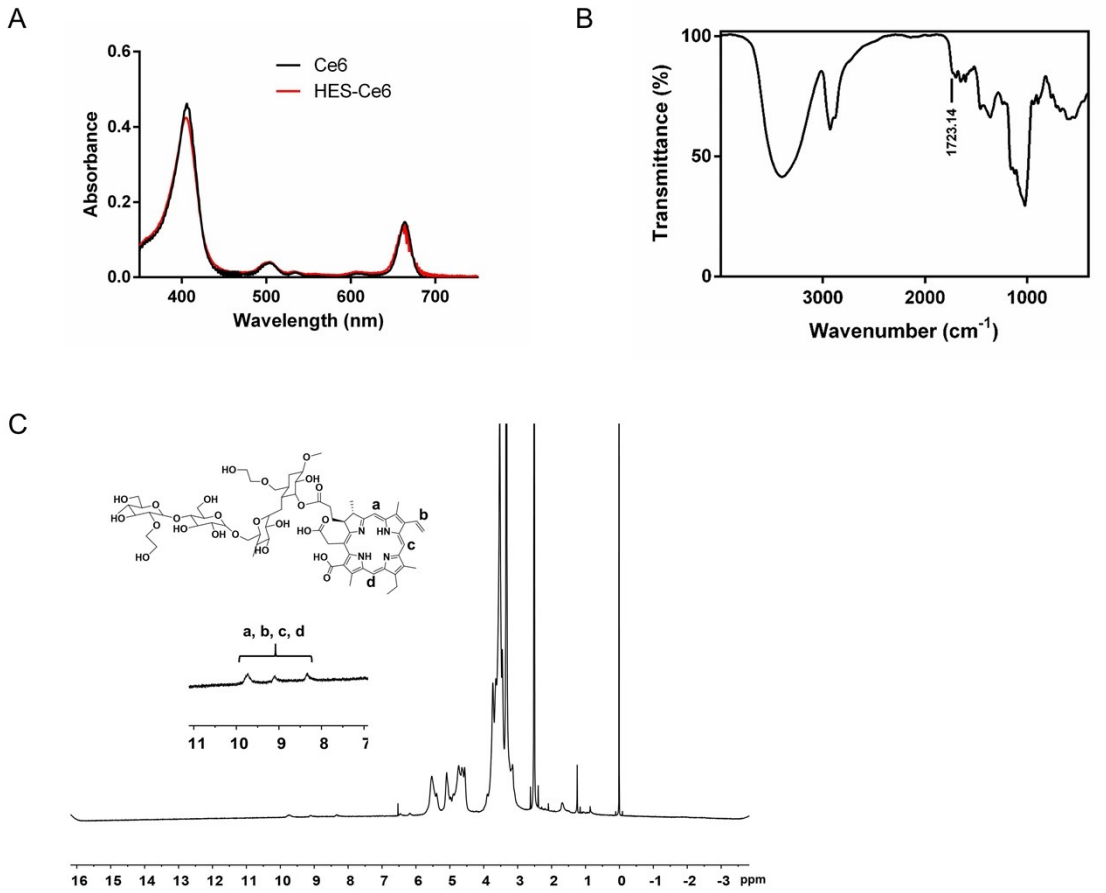

Fig. S1. Characterization of HES-Ce6 conjugates. (A) UV–vis absorption spectra of Ce6 and HES-Ce6. (B) FT-IR spectra of HES-Ce6. (C) ^{1}H NMR spectra of HES-Ce6.

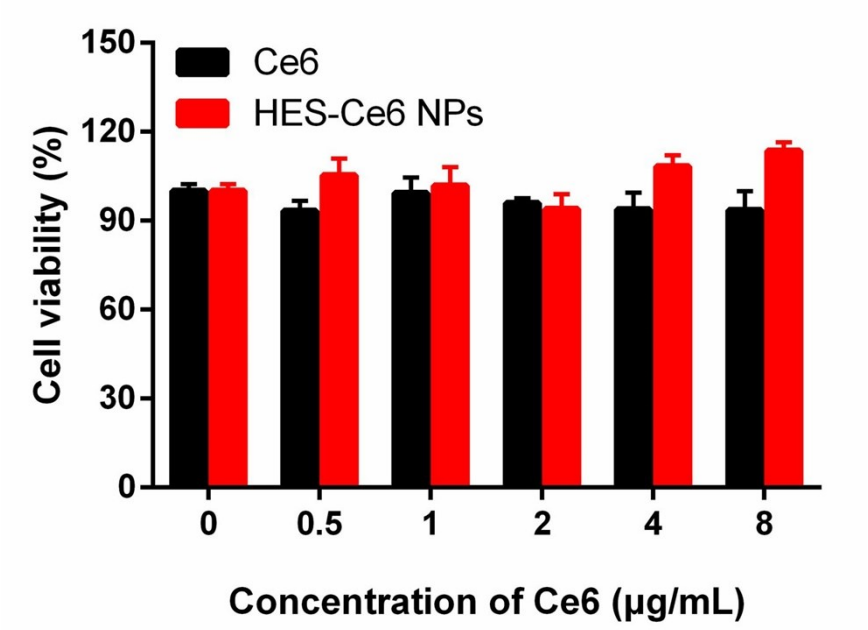

Fig. S2. Cytotoxicity of Ce6 and HES-Ce6 NPs without 660 nm laser irradiation. Data represent the mean ± SEM (n = 5).

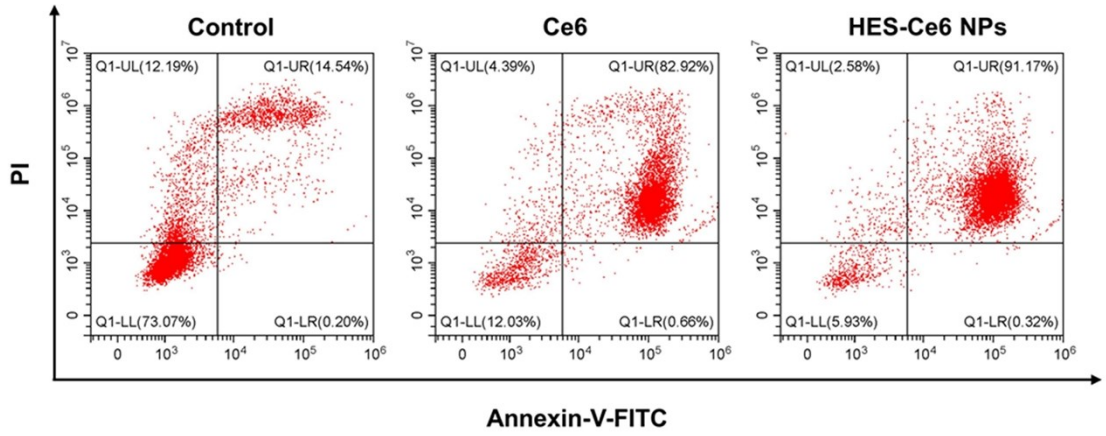

Fig. S3. Apoptosis of 4T1 cells treated with Ce6 and HES-Ce6 NPs （4 μg/mL as Ce6) after 660 nm laser irradiation (0.1 W/cm^2 , 2 min).

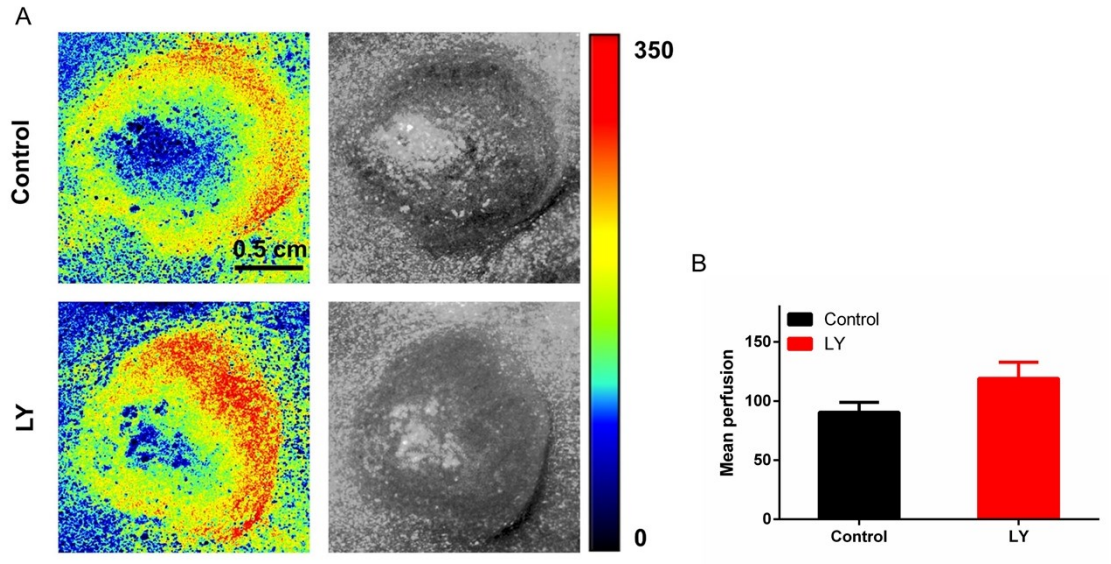

Fig. S4. LY enhanced tumor blood perfusion in 4T1 tumor bearing mice. (A) Representative images of blood perfusion in tumors and (B) quantification of blood perfusion. The scale bar is 0.5 cm. Data represent the mean ± SEM (n = 5).

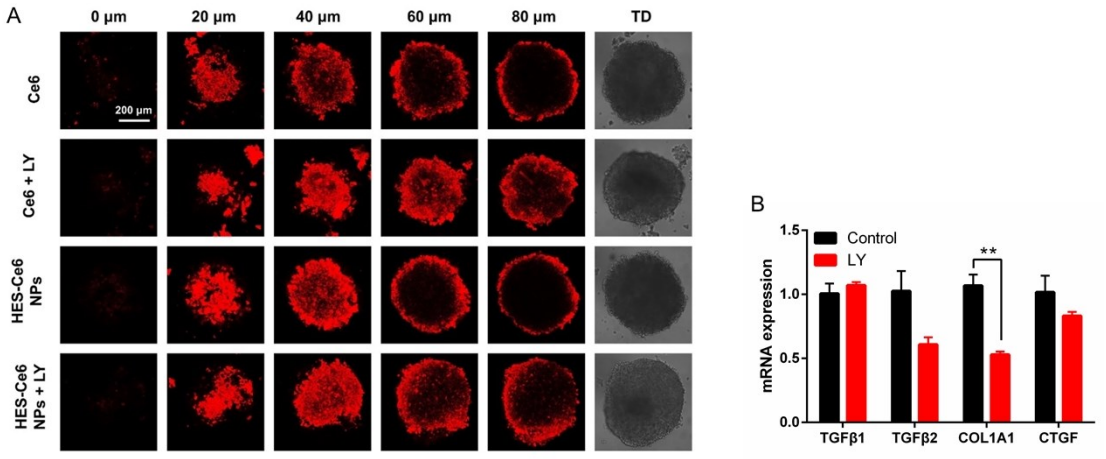

Fig. S5. LY improved drug penetration in stroma-rich 3D tumor spheroid. (A) Ce6 and HES-Ce6 NPs (2 μg/mL as Ce6) penetration in NIH 3T3/4T1 tumor spheroids by CLSM after incubation with LY (3 μg/mL). The scale bar is 200 μm. (B) mRNA expression of TGFβ1, TGFβ2, COL1A1 and CTGF in NIH 3T3/4T1 tumor spheroid after incubation with LY (3 μg/mL). $^{**}p < 0.01$. Data represent the mean ± SEM (n = 3).

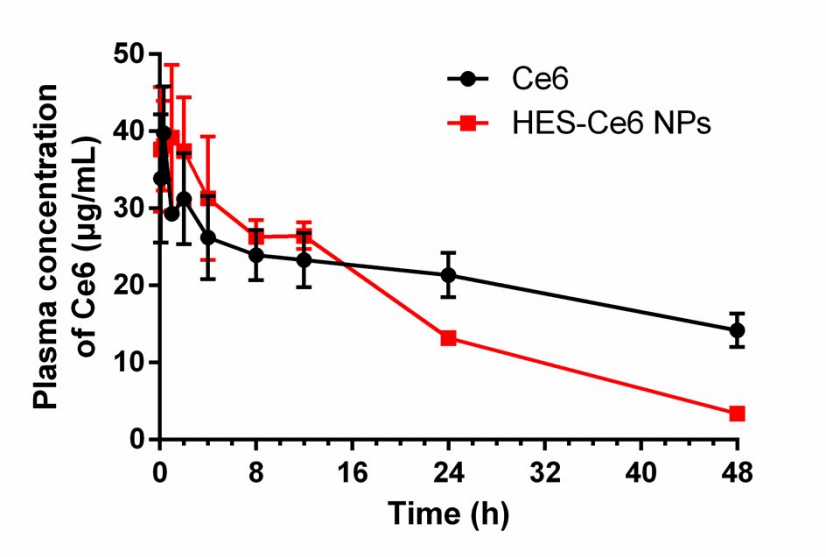

Fig. S6. Drug plasma concentration-time profiles of Ce6 and HES-Ce6 NPs after intravenous administration in rats. Data represent the mean ± SEM (n = 4).

Table S1. Pharmacokinetic parameters of Ce6 and HES-Ce6 NPs after intravenous administration in rats. Data represent the mean ± SEM (n = 4).

Parameters	Ce6	HES-Ce6 NPs
Dosage (mg Ce6/kg)	5	5
C_{max} (μg/mL)	41.830 ± 9.592	46.615 ± 5.778
$t_{1/2}$ (h)	43.233 ± 18.072	11.780 ± 1.326[a]
CL (L/h/kg)	0.002 ± 0.001	0.005 ± 0.001[a]
AUC $_{(0\rightarrow t)}$ (mg·h/L)	1038.204 ± 102.363	734.887 ± 119.988[a]

[a] $p < 0.05$ compared with Ce6. C_{max}, maximum plasma concentration. $t_{1/2}$, elimination half-life time. CL, clearance rate. AUC, area under curve.

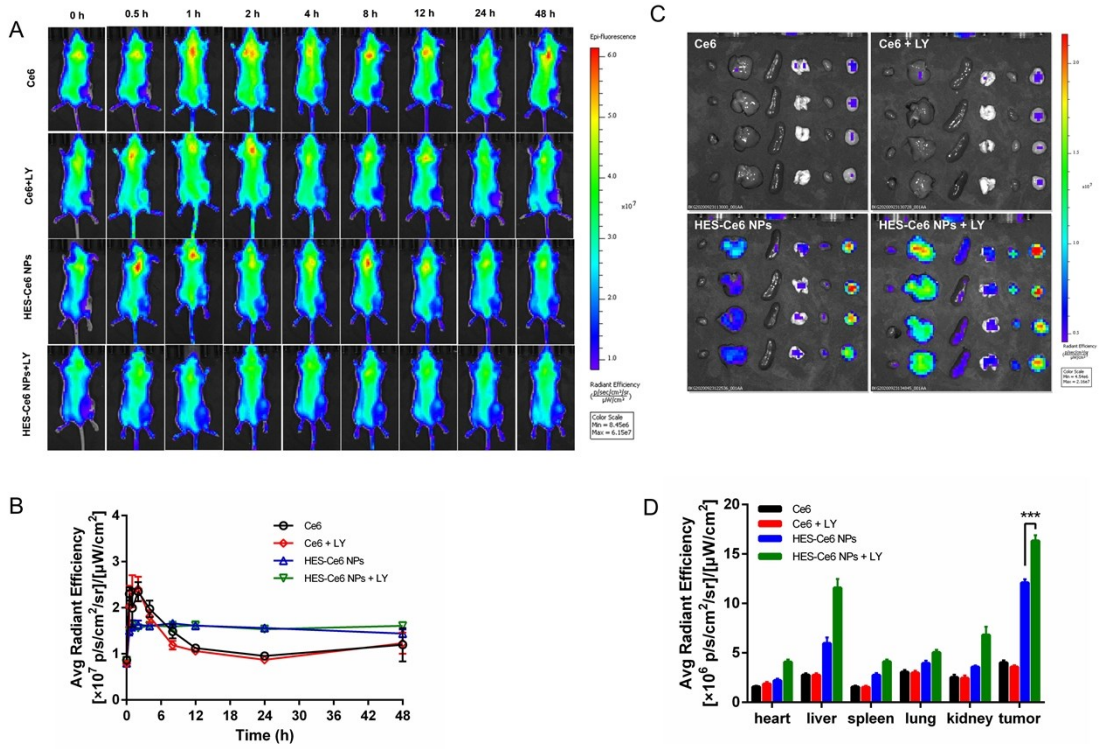

Fig. S7. LY promoted tumor accumulation of HES-Ce6 NPs. (A) *In vivo* fluorescent images of 4T1 tumor bearing mice and (B) quantification of fluorescent intensity of tumors at pre-determined time points (0, 0.5, 1, 2, 4, 8, 12, 24, 48 h) after mice were *i.v.* injected with Ce6 and HES-Ce6 NPs (5 mg/kg as Ce6). (C) Ex vivo fluorescent images and (D) quantification of fluorescent intensity of major organs and tumors 48 h after mice were *i.v.* injected with Ce6 and HES-Ce6 NPs. ***$p < 0.001$. Data represent the mean ± SEM (n = 4).

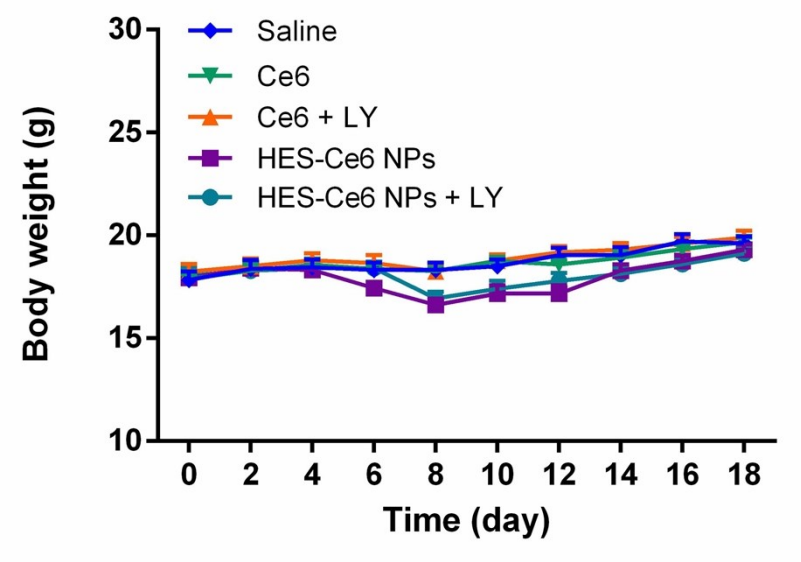

Fig. S8. Body weight of 4T1 tumor bearing mice with different treatments. Data represent the mean ± SEM (n = 8).

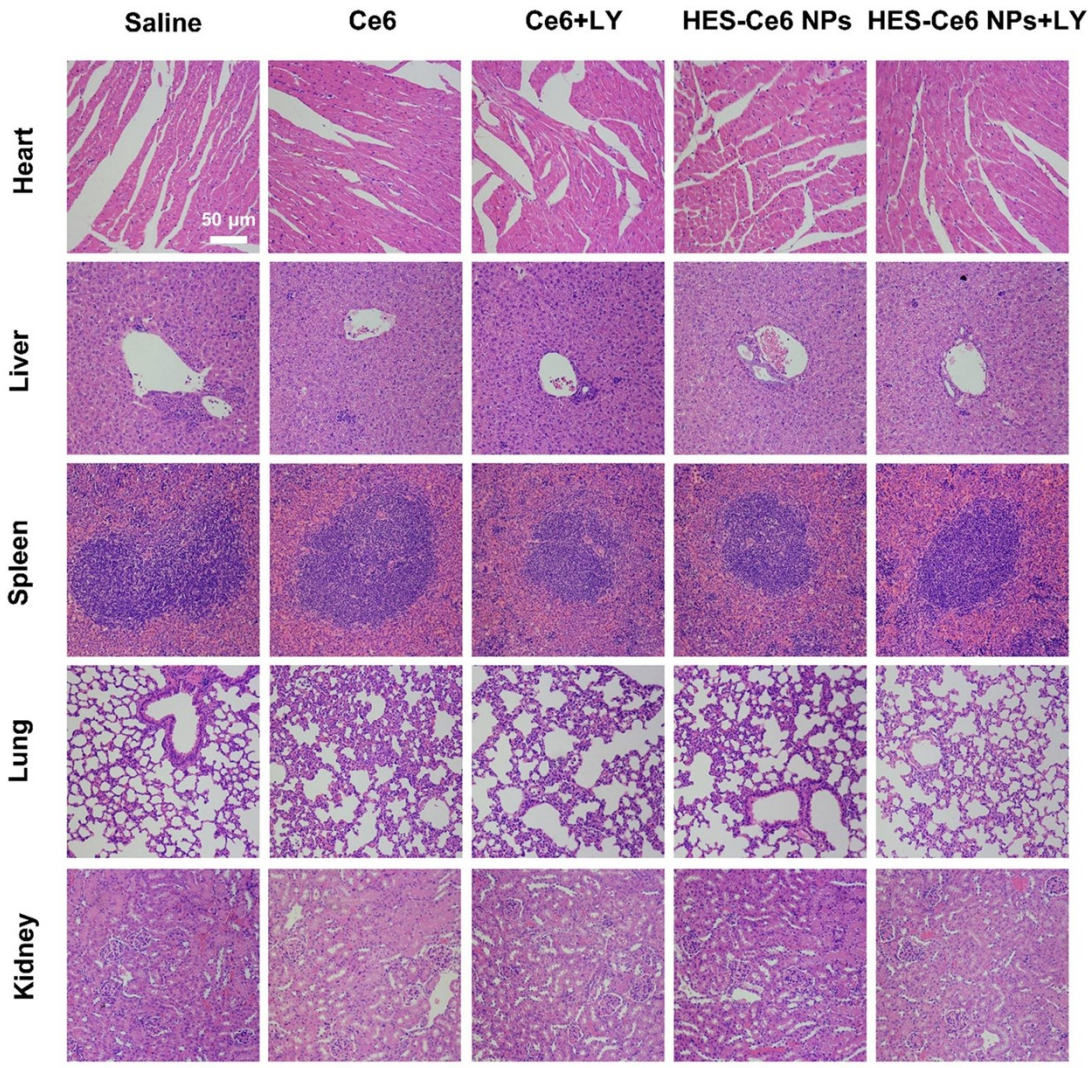

Fig. S9. H&E staining of major organs at the end of the *in vivo* antitumor experiment. The scale bar is 50 μm.

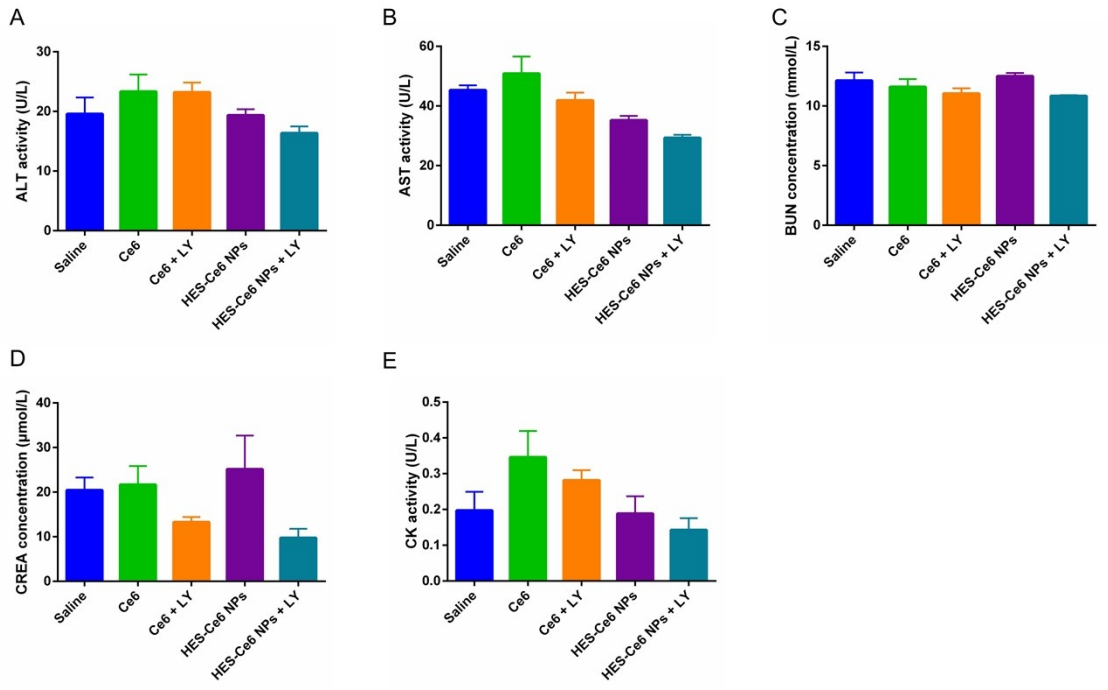

Fig. S10. Biocompatibility evaluation of combination therapy. Serological analysis of (A) alanine aminotransferase (ALT), (B) aspartate aminotransferase (AST), (C) blood urea nitrogen (BUN), (D) creatinine (CREA) and (E) creatine kinase in 4T1 tumor-bearing mice with different treatments. Data represent the mean ± SEM (n = 5).