Supporting Information

Tumor-penetrating iron oxide nanoclusters for T_1/T_2 dual mode MR imaging-guided combination therapy

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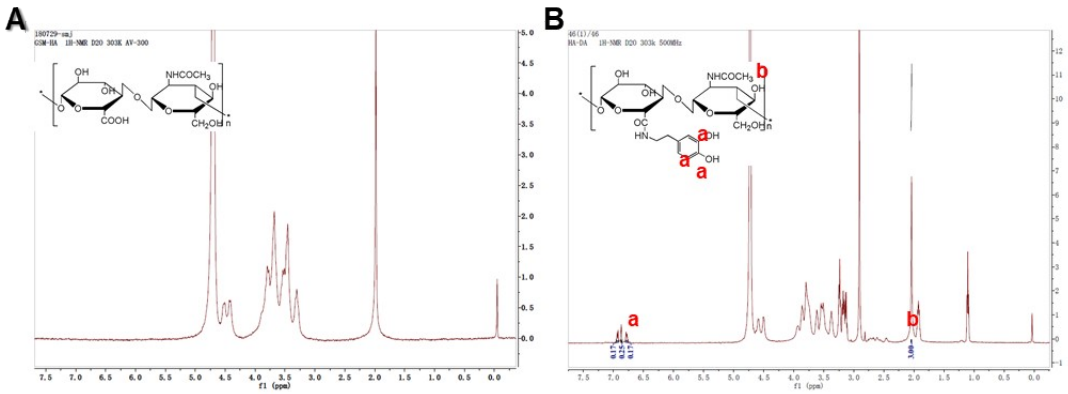


Figure S1. The 1H-NMR spectra of HA (A) and HA-DA (B).

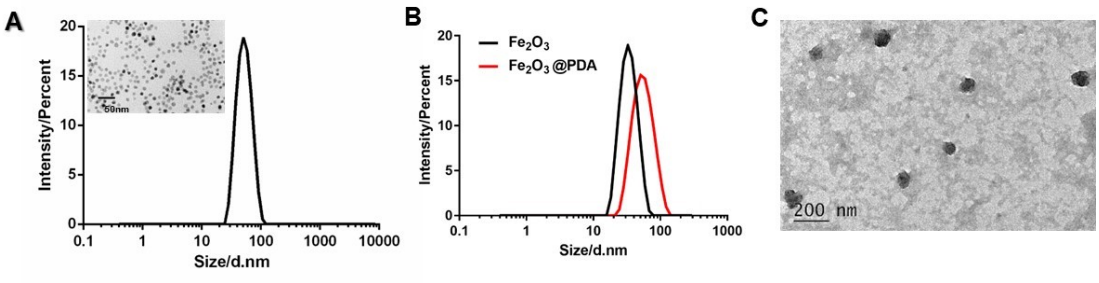


Figure S2. (A) Frequency curve of size distribution of Fe_2O_3 nanoparticles. Inset: TEM image of Fe_2O_3 nanoparticles. (B) Frequency curve of size distribution of Fe_2O_3 nanoparticles and Fe_2O_3@PDA nanoparticles. (C) TEM image of Fe_2O_3@PDA.

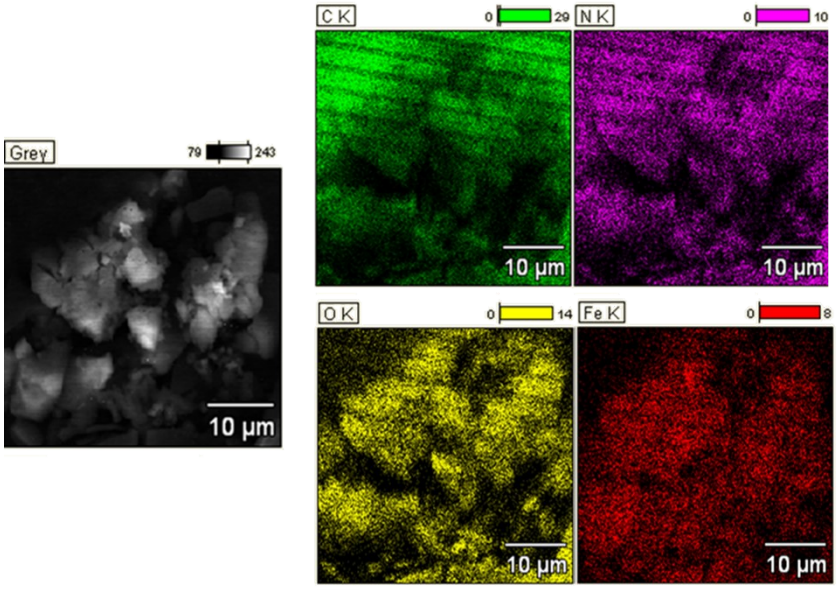


Figure S3. FESEM image and corresponding elemental composition images of Fe_2O_3@PFH NCs.

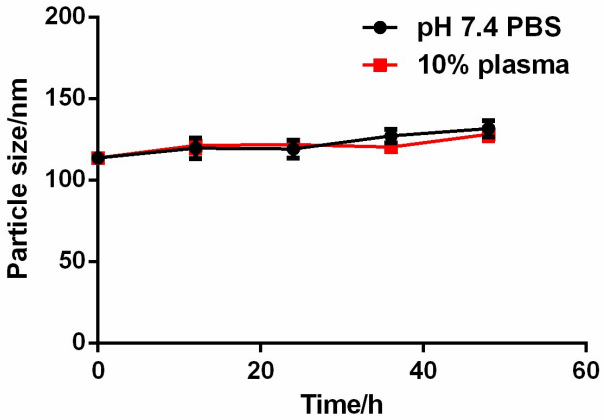


Figure S4. Change in particle size of Fe_2O_3@PFH nanocluster after incubating in PBS buffer solution (pH 7.4) and 10 % plasma.

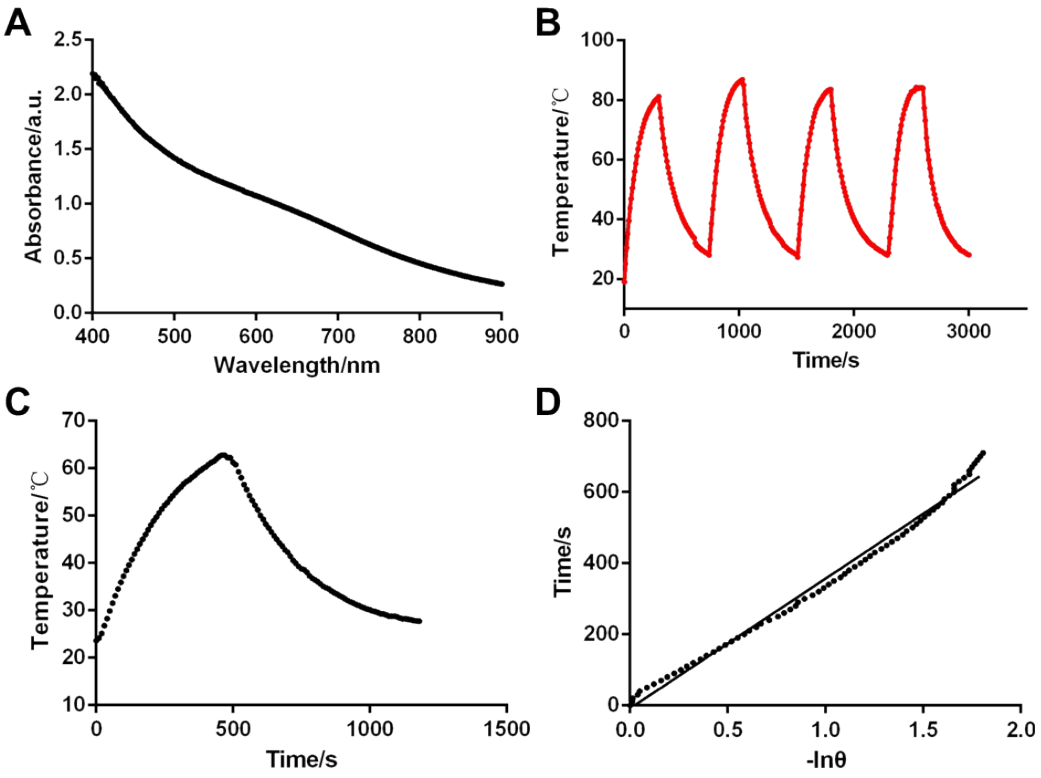
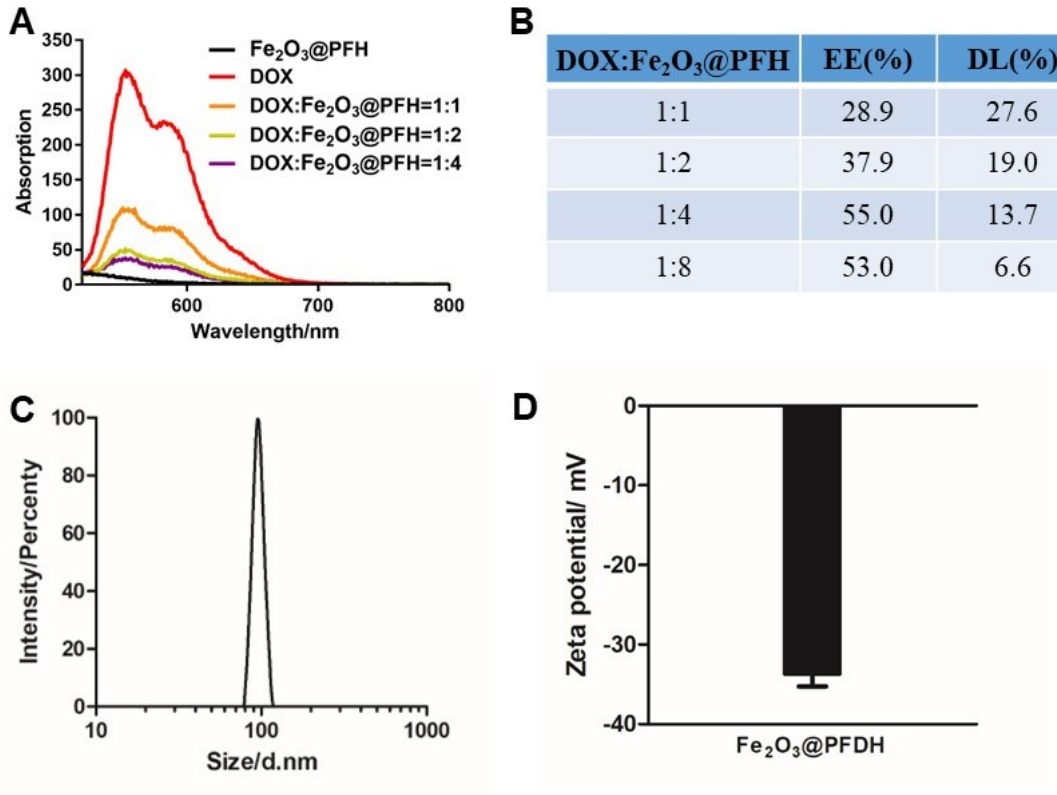


Figure S5. (A) UV-vis spectra of the Fe_2O_3@PFH nanocluster. (B) The temperature change of the Fe_2O_3@PFH NCs solution (0.50 mg/mL) upon four circles of NIR laser irradiation (808 nm, 1.6 W/cm^2) that was repeated on and off at a cycle of 750 s. (C) The temperature change of the Fe_2O_3@PFH nanocluster under laser irradiation (808 nm, 1.6 W/cm^2). The laser was switched off until the temperature reached the peak. (D) Linear time data from the cooling period (after 500 s in Figure S5C) vs. negative natural logarithm of driving force temperature. The slope of the linear line was the time constant for heat transfer of the system (364.72 s).



DOX:Fe_2O_3@PFH	EE(%)	DL(%)
1:1	28.9	27.6
1:2	37.9	19.0
1:4	55.0	13.7
1:8	53.0	6.6

Figure S6. (A) Fluorescence measurement of mixture of Fe_2O_3@PFH and DOX with different weight ratio at 488 nm. (B) Encapsulation efficiency and drug loading content of Fe_2O_3@PFDH with the different ratio (w/w). (C) Particle size distribution and (D) zeta potential of Fe_2O_3@PFDH detected by DLS.

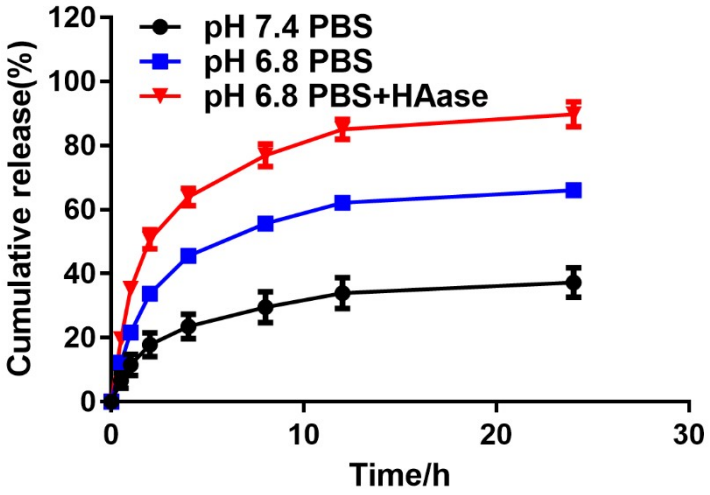


Figure S7. The release curve of DOX from Fe_2O_3@PFDH NCs under the different conditions of pH 7.4, pH 6.8, PBS or pH 6.8 PBS with HAase (1 mg/mL) at 37 °C.

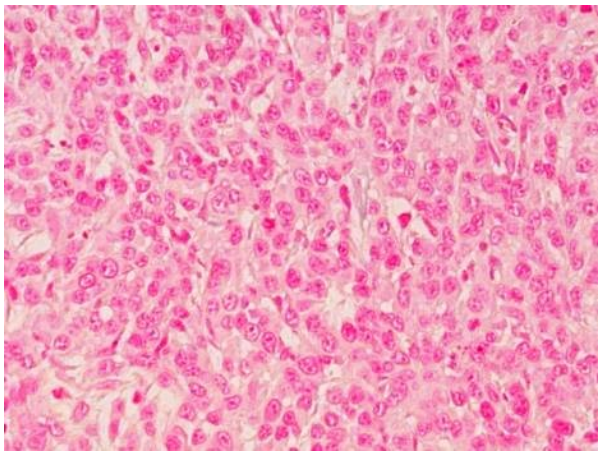


Figure S8. Prussian blue staining images of the tumor section from mice upon 24 h of injection of saline.

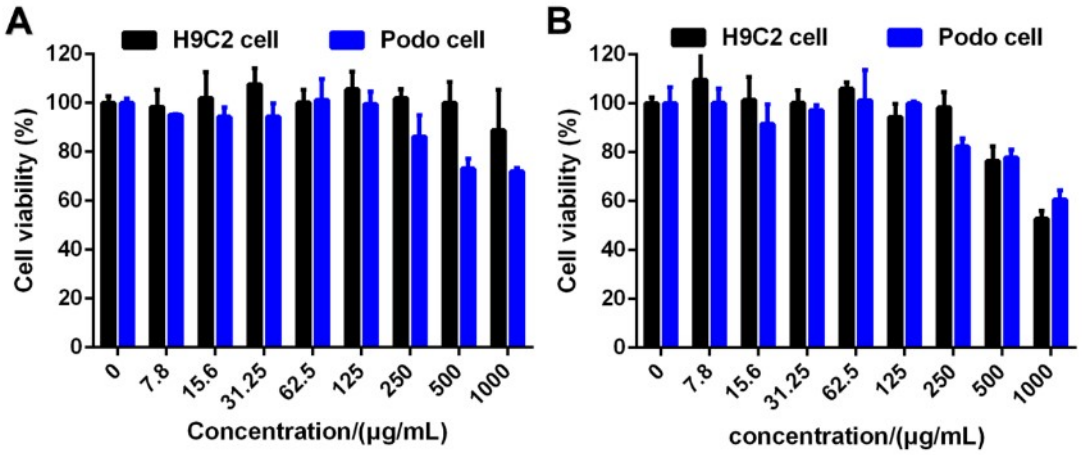


Figure S9. Cell viability of H9C2 and Podo cells after incubation with different concentrations of Fe_2O_3@PFH(A) and HA-DA(B).

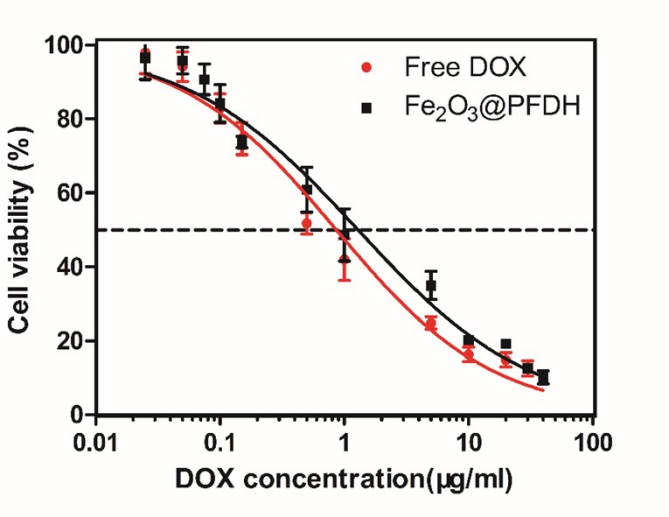


Figure S10. Cell viability of 4T1 cells treated by free DOX and Fe_2O_3@PFDH after incubation for 24h. (n=3)

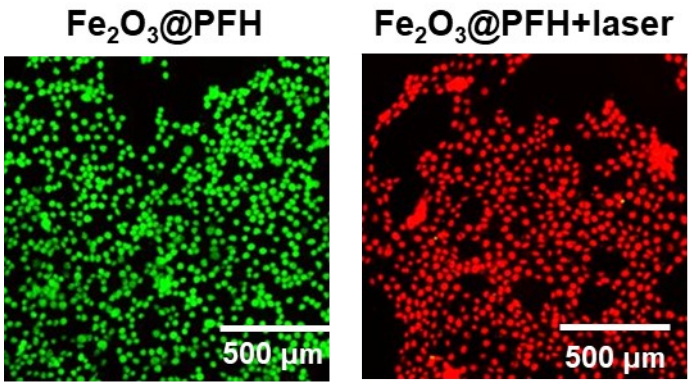


Figure S11. Fluorescence images of calcein AM (live cells, green) and PI (dead cells, red) co-stained 4T1 cells after treatments with 0.2 mg/mL of Fe_2O_3@PFH NCs with or without laser irradiation.

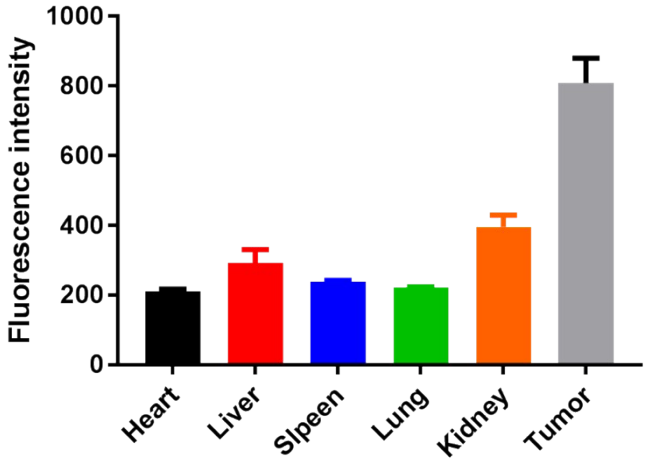


Figure S12. The fluorescence intensity of heart, liver, spleen, lung, kidneys and tumor isolated at 24 h post-injection of the Cy7-Fe_2O_3@PFH NCs.

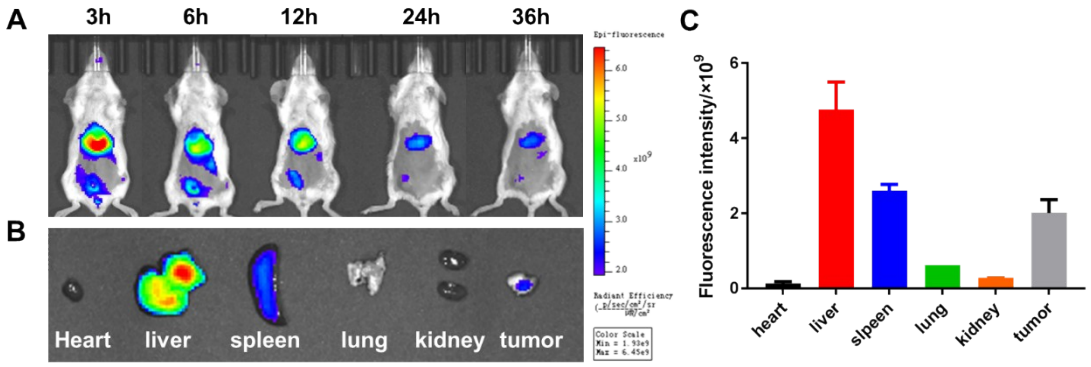


Figure S13. The distribution of the free Cy7-NHS ester with tween 80 *in vivo*. (A) Images of mice following intravenous injection of the free Cy7. (B) Images of heart, liver, spleen, lung, kidneys and tumor isolated at 24 h post-injection of the free Cy7. (C) The corresponding fluorescence intensity.

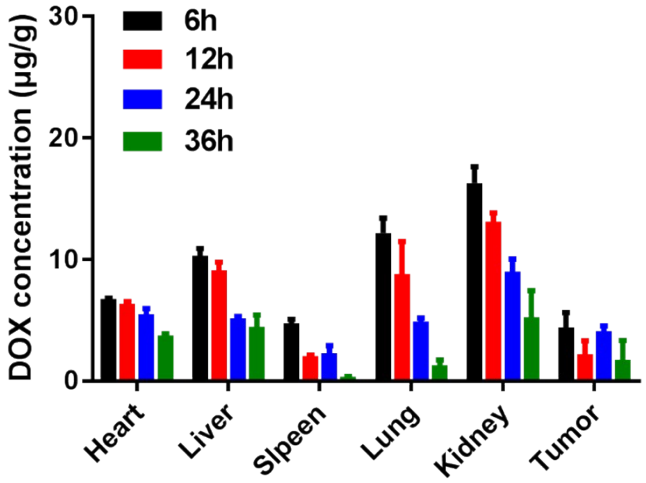


Figure S14. Content analysis of DOX in major organs and tumor isolated at predetermined time post-injection of the free DOX.

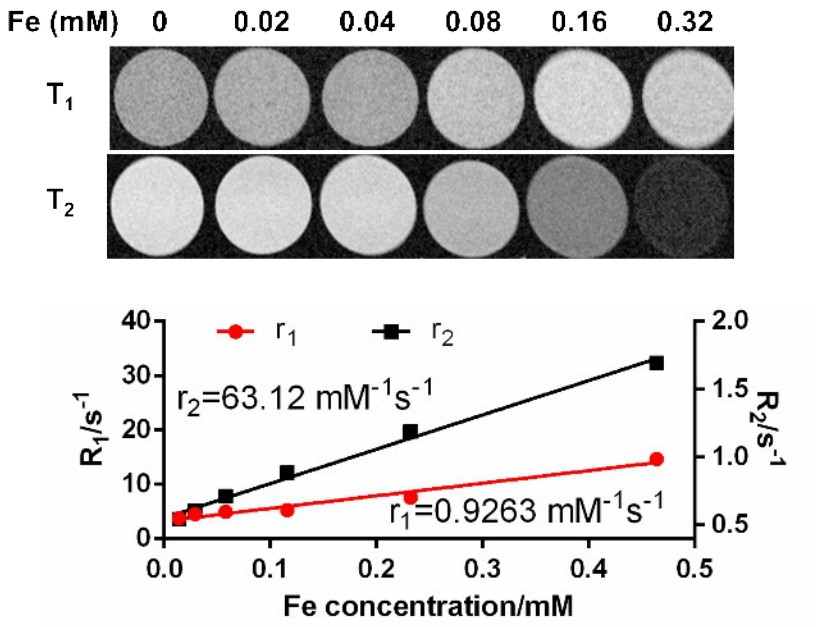


Figure S15. The reciprocal values of relaxation times (R_1, R_2) of Fe_2O_3 nanoparticle versus different concentrations of Fe^{3+}, and the relaxivity values (r_1, r_2) were obtained from the slopes of linear fits of experimental data.

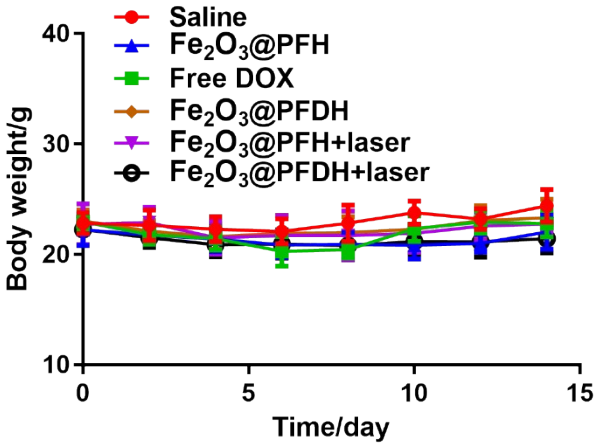


Figure S16. Body weight change of 4T1 tumor-bearing mice treated with different preparations.

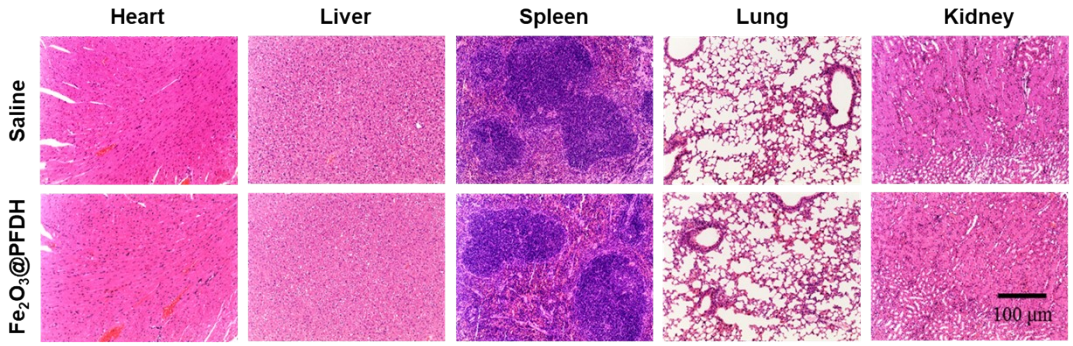


Figure S17. H&E staining images of major organs from healthy mice treated with tested dose of the Fe_2O_3@PFDH NCs and saline.

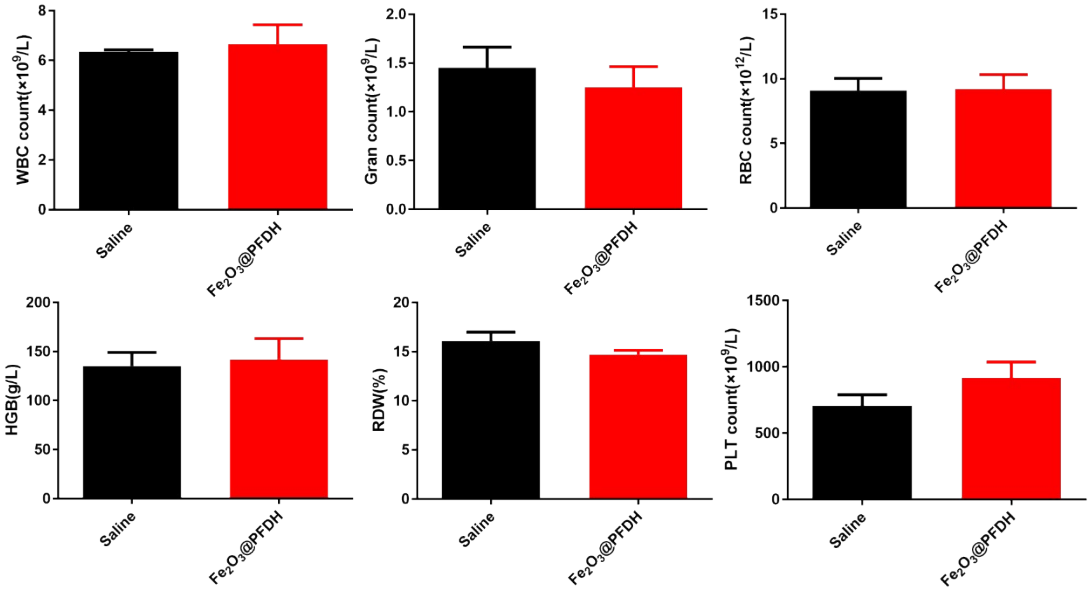


Figure S18. Hematology data of the mice treated with saline and Fe_2O_3@PFDH.