Supplement Information

Magnetic Reactive Oxygen Species Nanoreactor for Switchable Magnetic Resonance Imaging Guided Cancer Therapy Based on pH-Sensitive Fe_5C_2@Fe_3O_4 Nanoparticles

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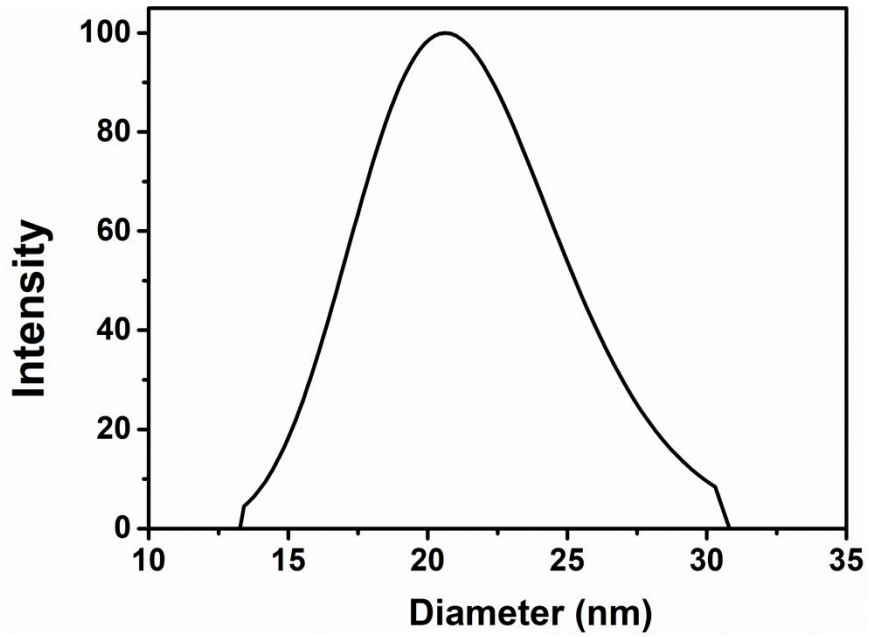


Figure S1. DLS spectrum of $Fe_5C_2@Fe_3O_4$ NPs.

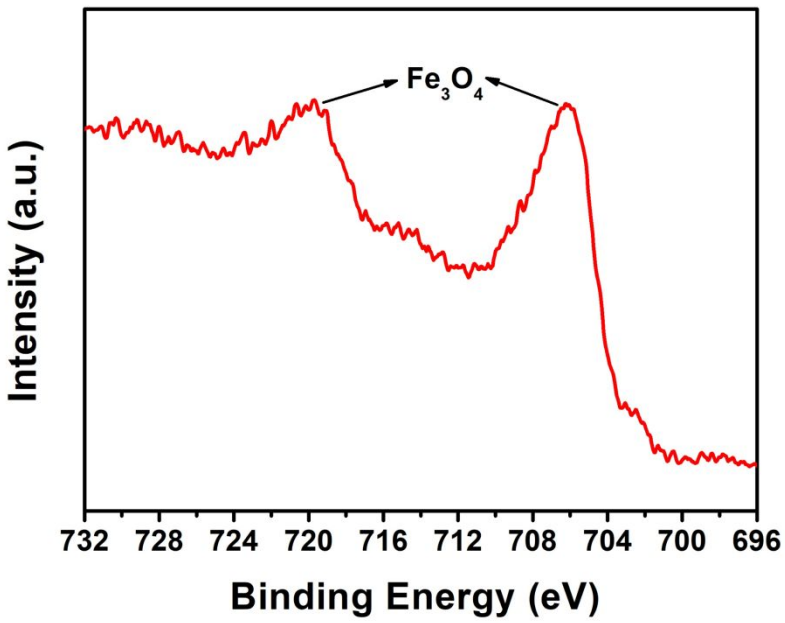


Figure S2. Fe 2p XPS spectrum of $Fe_5C_2@Fe_3O_4$ NPs.

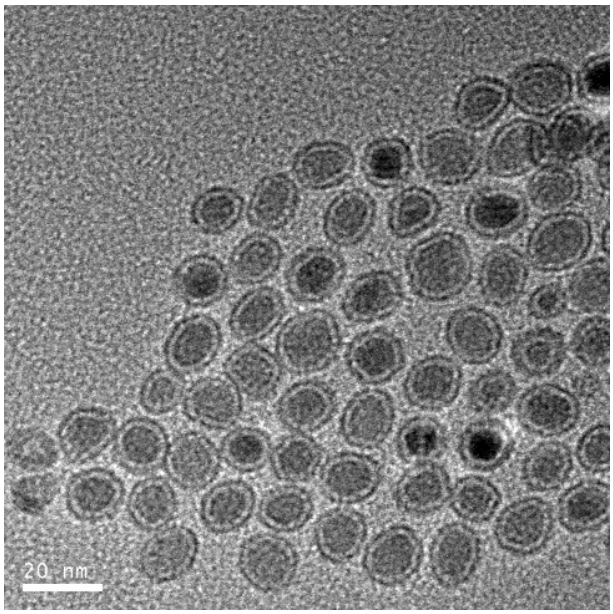


Figure S3. TEM image of $Fe_5C_2@Fe_3O_4$ NPs after 7 days storage in air.

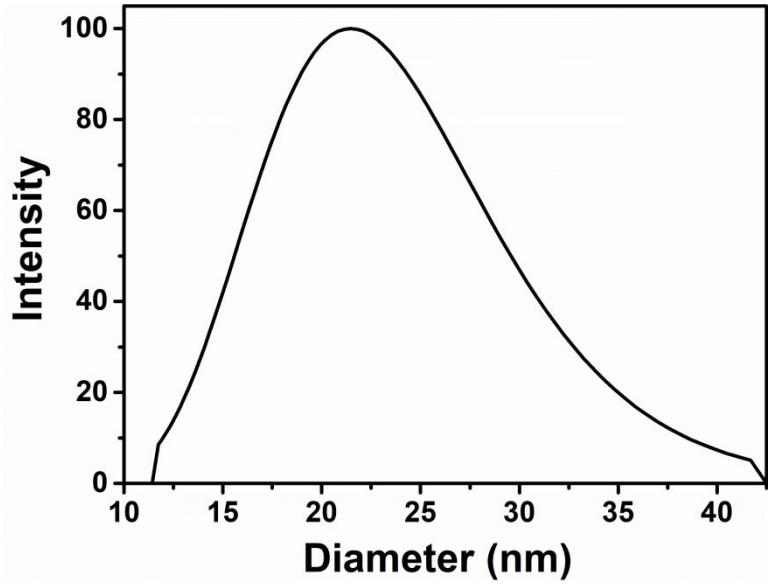


Figure S4. DLS spectrum of $Fe_5C_2@Fe_3O_4$ NPs after 7 days storage in air.

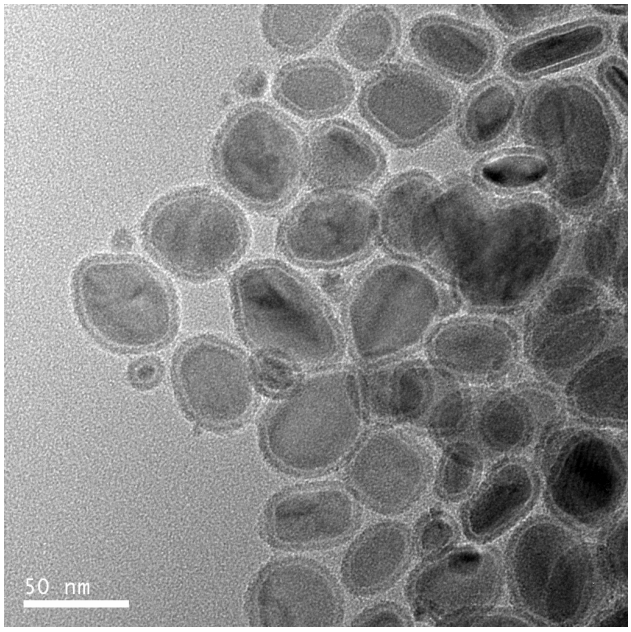


Figure S5. TEM image of 20 nm Fe_5C_2@C NPs.

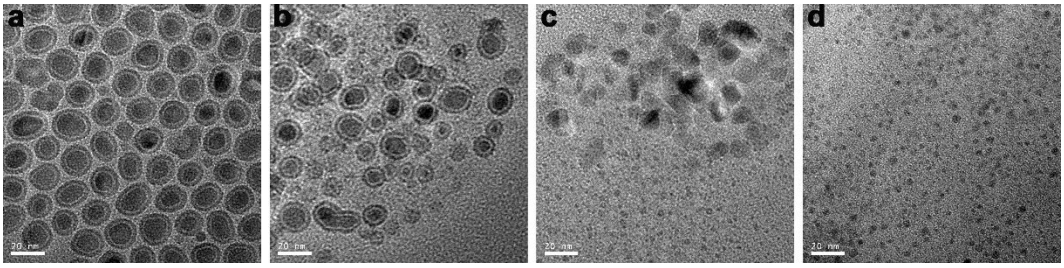


Figure S6. TEM image of PEG/Fe_5C_2@Fe_3O_4 NPs by dispersing in pH 5.4 with different time (**a** 0h, **b** 1h, **c** 2h, **d** 4h).

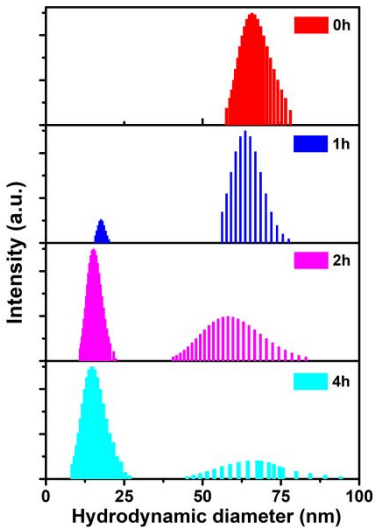


Figure S7. DLS spectrum of PEG/Fe_5C_2@Fe_3O_4 NPs dispersing in pH 5.4 with different time.

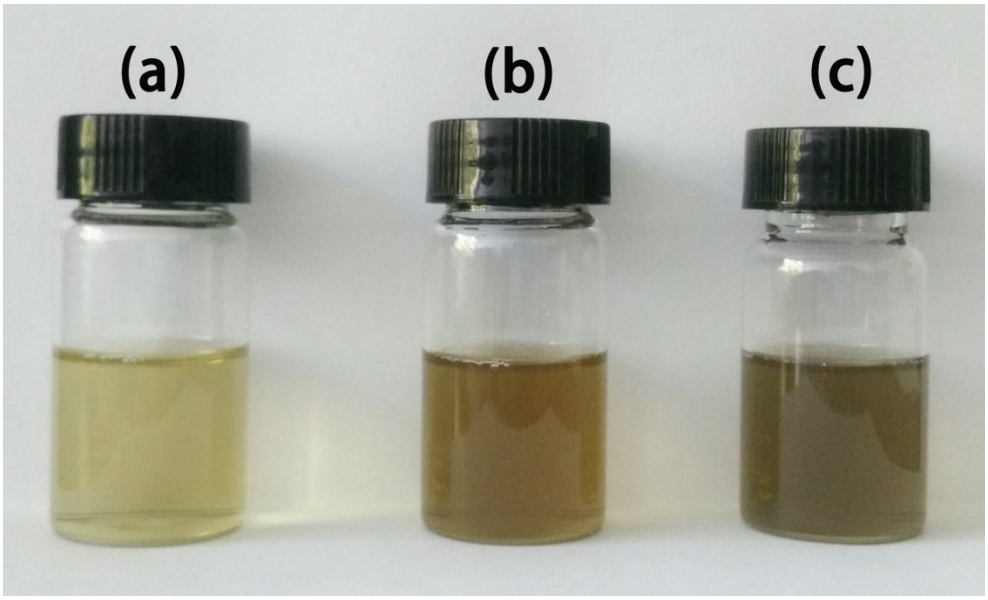


Figure S8. Photograph of PEG/Fe_5C_2@Fe_3O_4 NPs dispersing in (**a**) pH 5.4, (**b**) pH 6.5 and (**c**) pH 7.4 for 4 h.

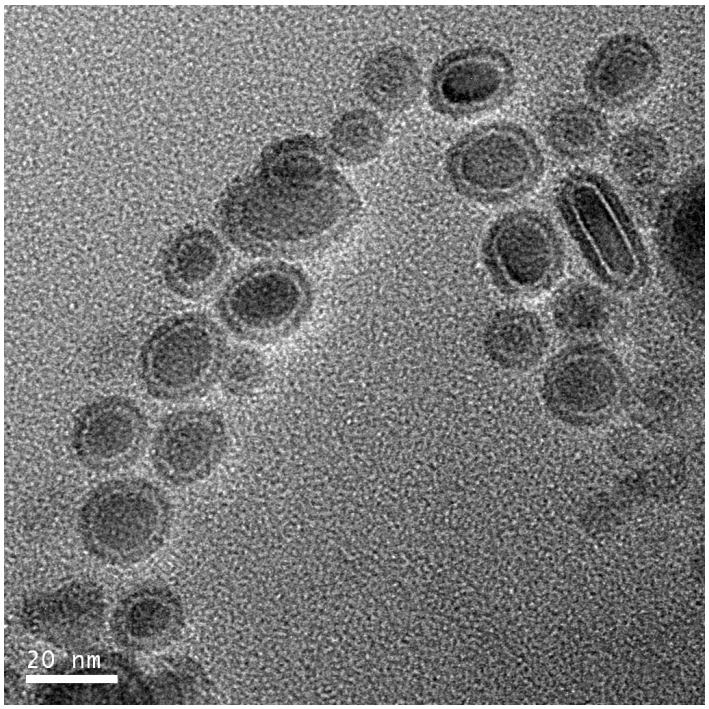


Figure S9. TEM image of PEG/Fe_5C_2@C NPs by dispersing in pH 5.4 solution for 4 h.

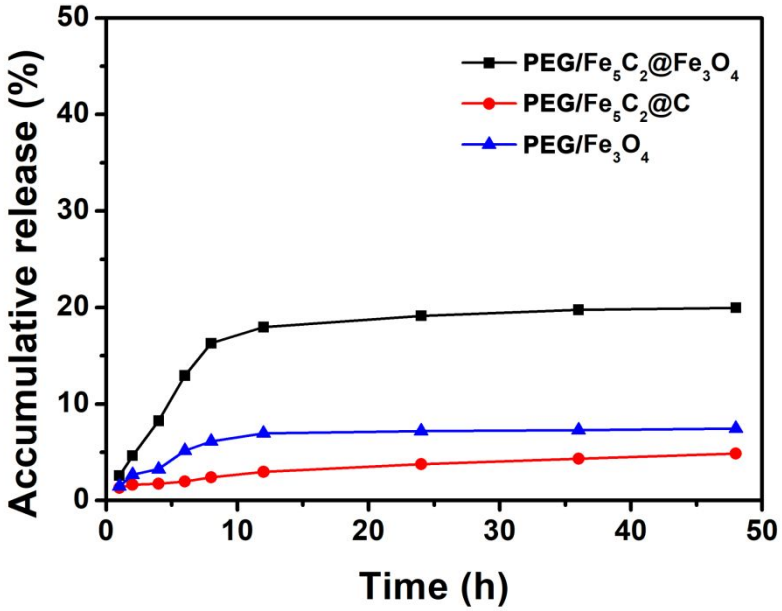


Figure S10. Accumulative iron ion release of PEG/Fe_5C_2@Fe_3O_4, PEG/Fe_5C_2@C and PEG/Fe_3O_4 NPs at pH 6.5.

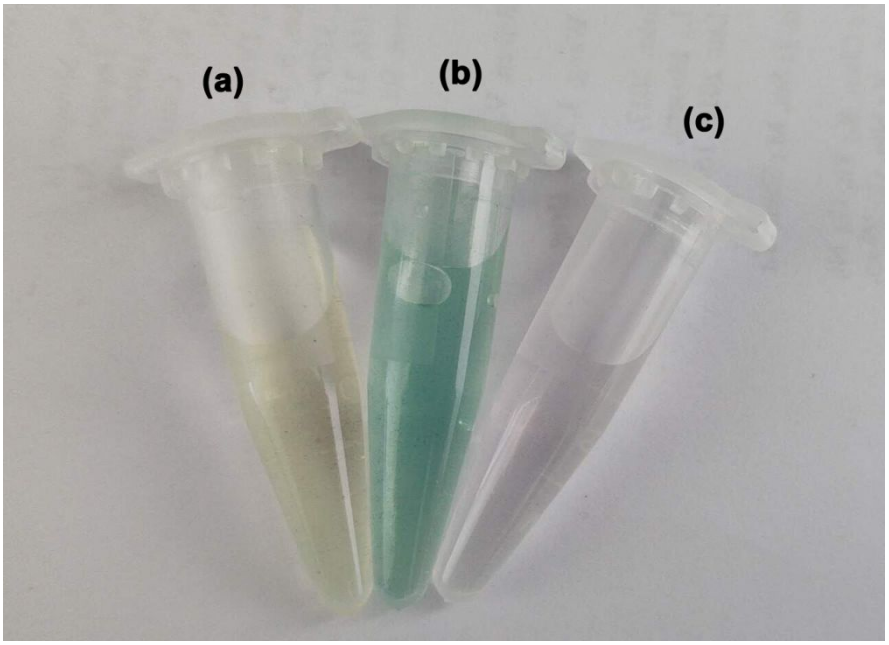


Figure S11. Photo of (**a**, **b**) potassium ferricyanide dispersed PEG/Fe_5C_2@Fe_3O_4 NPs solution at (**a**) pH 7.4 and (**b**) pH 5.4 for 24 h. (**c**) Photo of potassium thiocyanate dispersed PEG/Fe_5C_2@Fe_3O_4 NPs solution at pH 5.4 for 24 h.

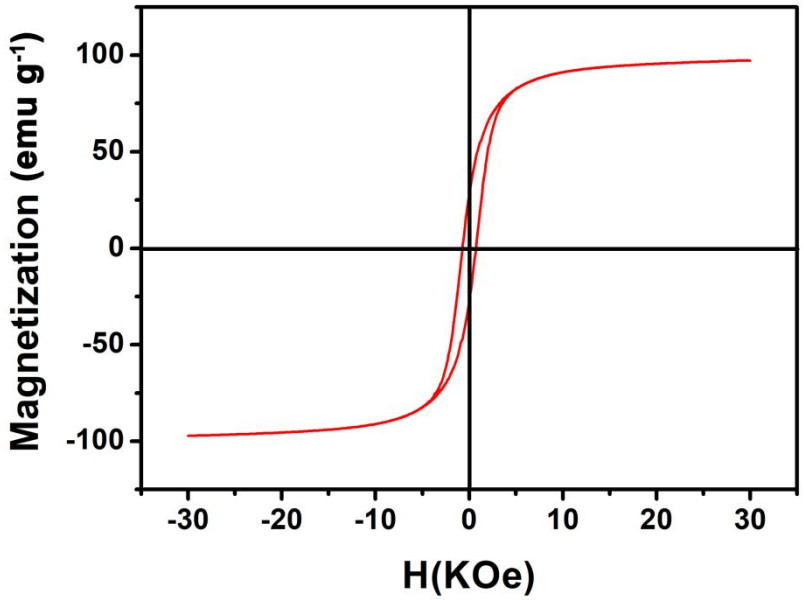


Figure S12. Room-temperature magnetic hysteresis loops of PEG/Fe_5C_2@Fe_3O_4 NPs.

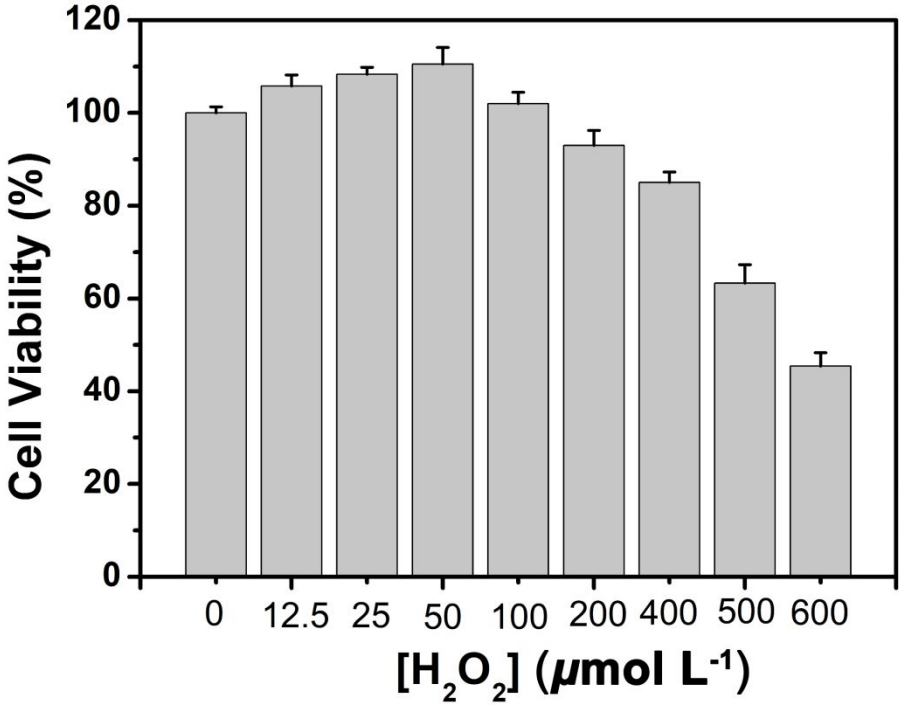


Figure S13. Cell viability of 4T1 cells after 24 h incubation with different concentrations of H_2O_2.

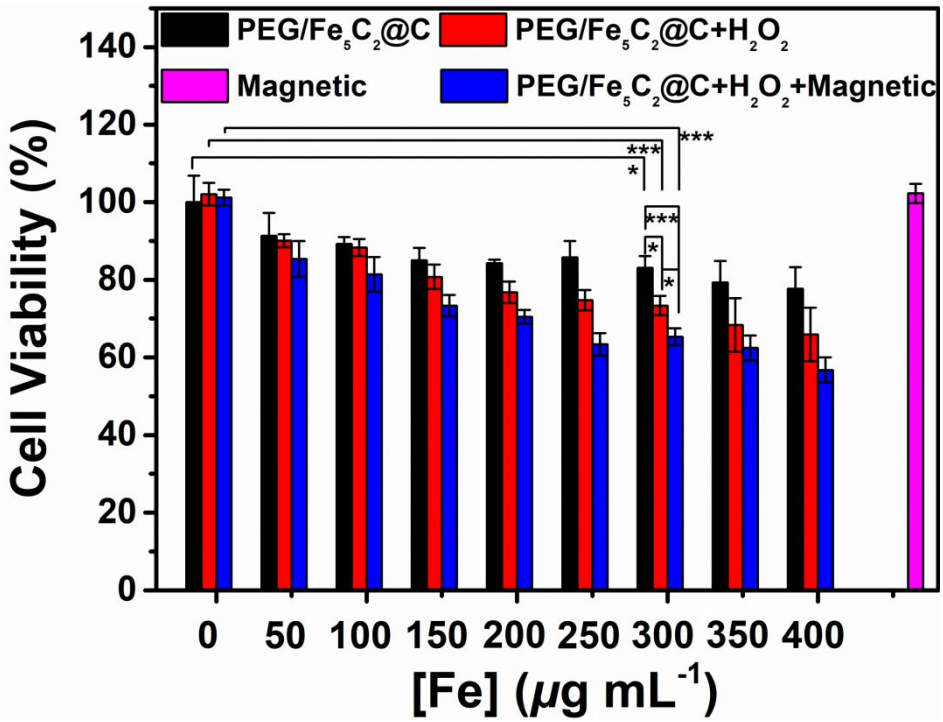
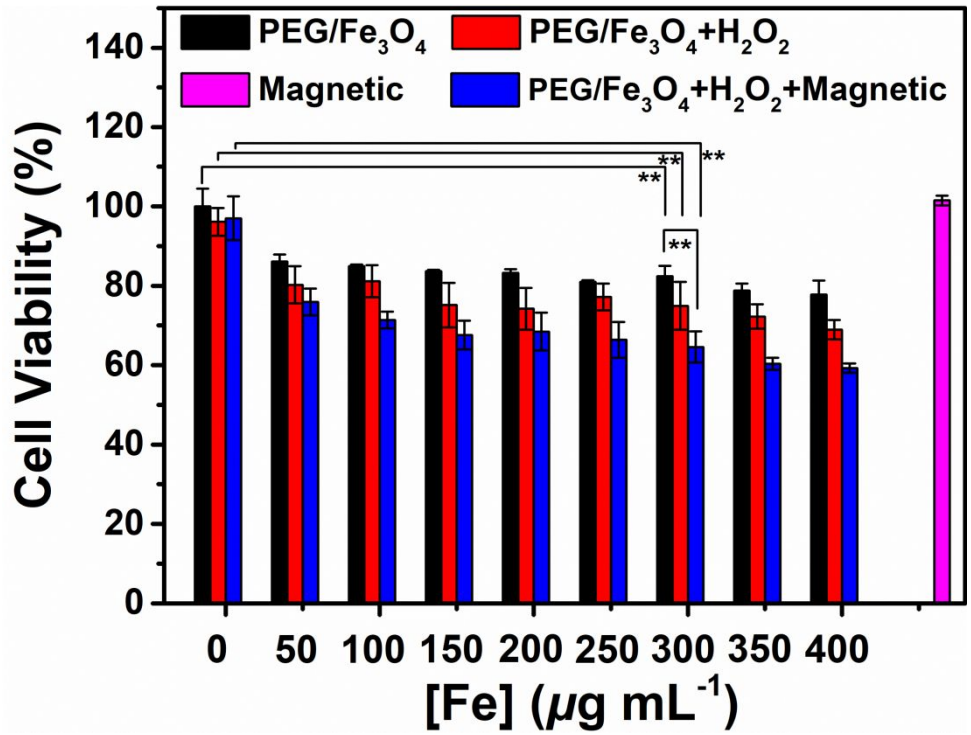


Figure S14. Cell viability of 4T1 cells after 24 h incubation with PEG/Fe_5C_2@C NPs or PEG/Fe_5C_2@C NPs + H_2O_2 (50 μmol L^{-1}) with or without magnetic field. (n = 6, mean ± *s.d.*, $^{**}p < 0.01$).



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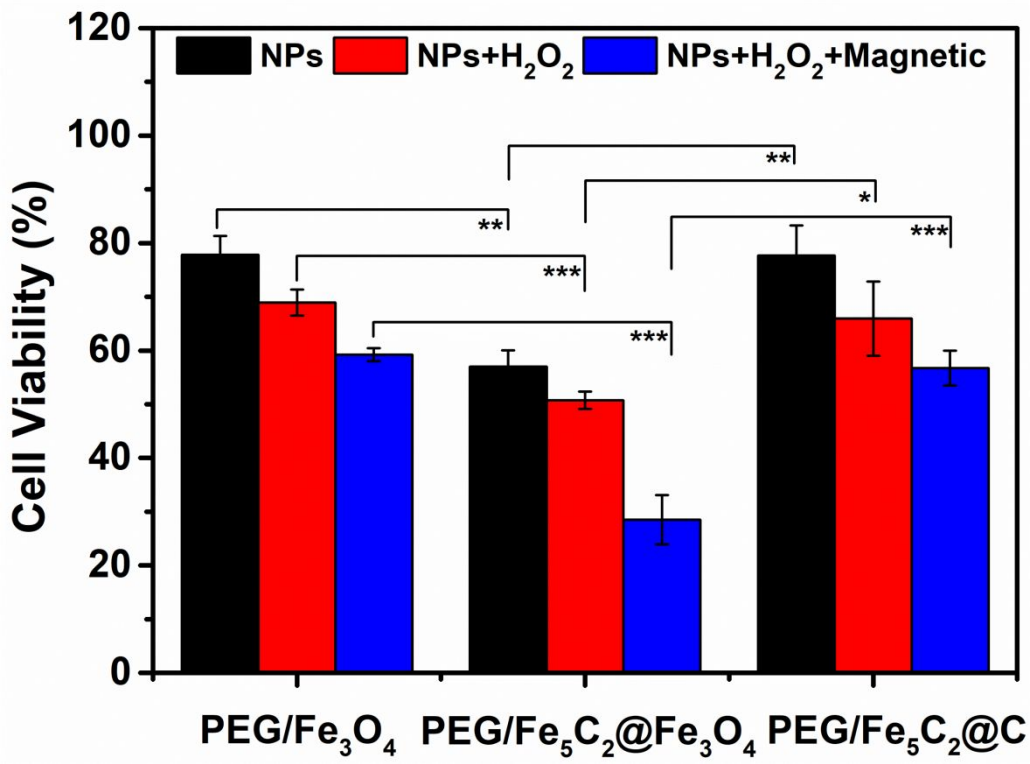

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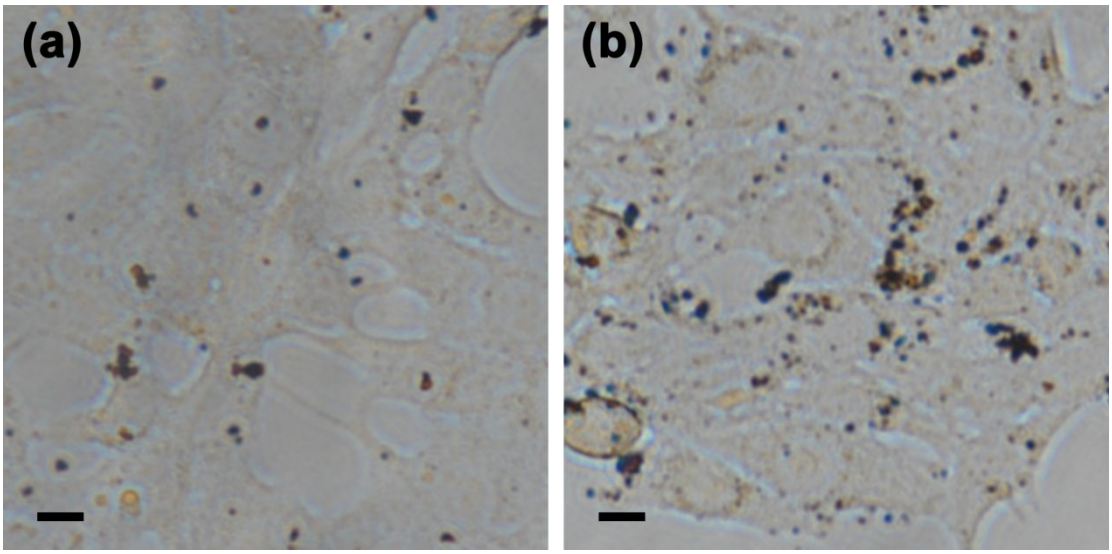


Figure S17. The representative Prussian blue staining of 4T1 cells (**a**) without and (**b**) with magnetic targeting. Scale bars are 20 μm.

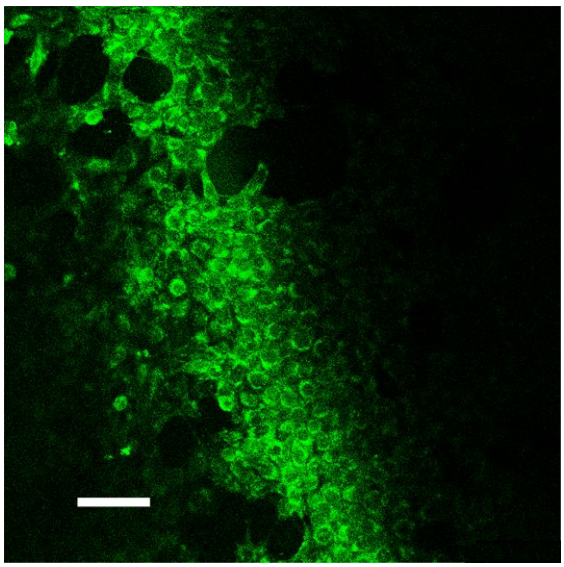


Figure S18. Fluorescence image of DCFH-DA labeled 4T1 cells treated by PEG/Fe_5C_2@Fe_3O_4 NPs + H_2O_2 (50 μmol L^{-1}) under magnetic targeting. Scale bars are 75 μm.

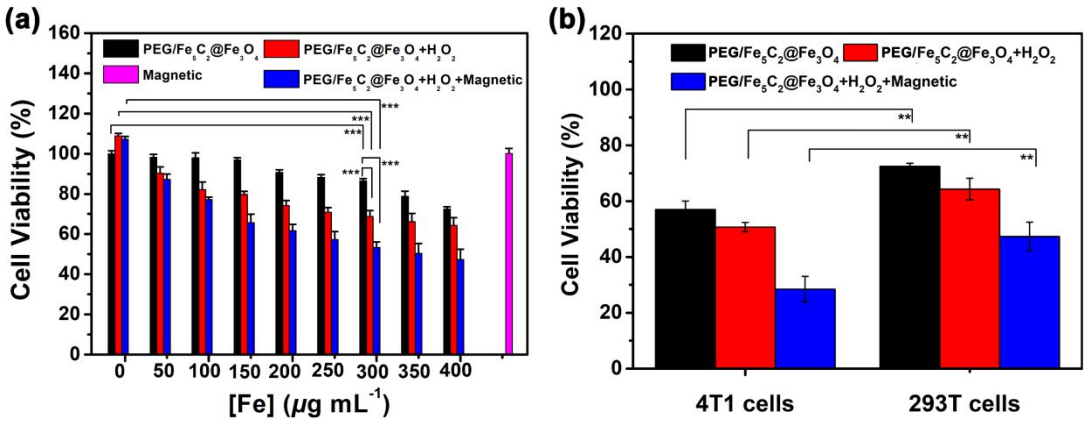
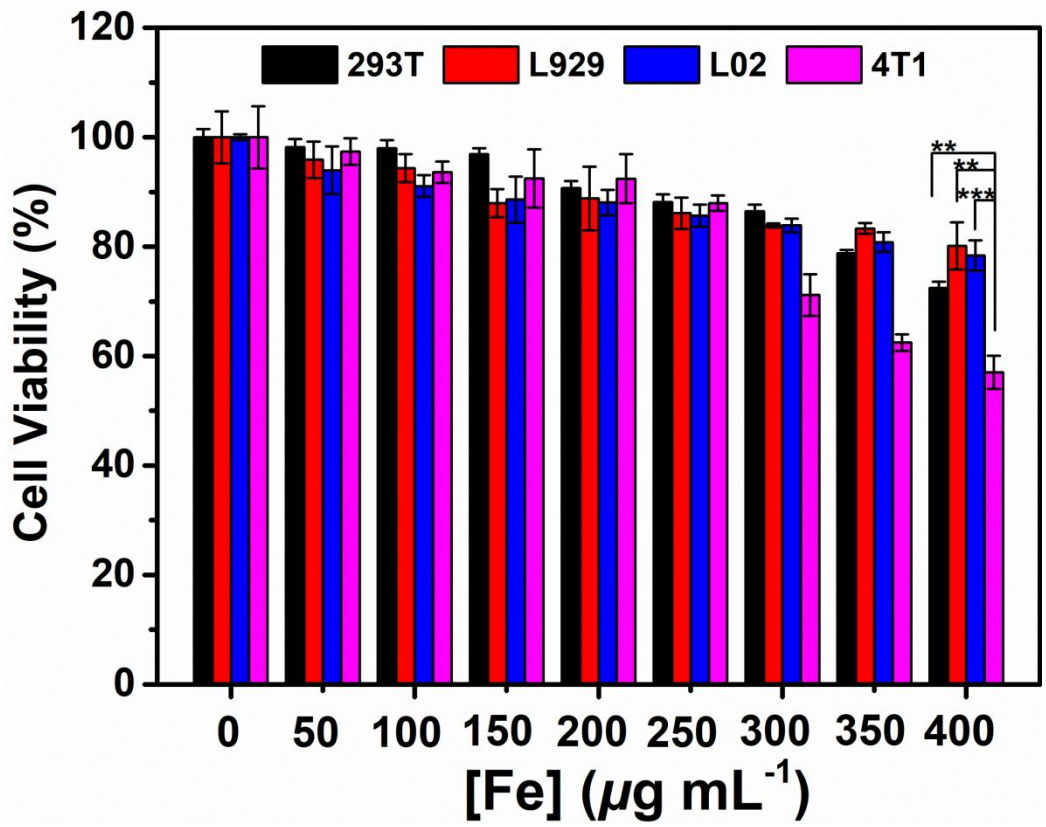


Figure S19. (**a**) Cell viability studies in 293T cells model after incubation with PEG/Fe_5C_2@Fe_3O_4 NPs or PEG/Fe_5C_2@Fe_3O_4 NPs + H_2O_2 (50 μmol L^{-1}) with or without magnetic field. (**b**) Cell viability of 4T1 or 293T cells after 24 h incubation with different NPs in different conditions at concentration of 400 μg Fe mL^{-1}. The H_2O_2 concentration was 50 μmol L^{-1}. (n = 6, mean ± *s.d.*, $^{**}p < 0.01$, and $^{***}p < 0.001$).



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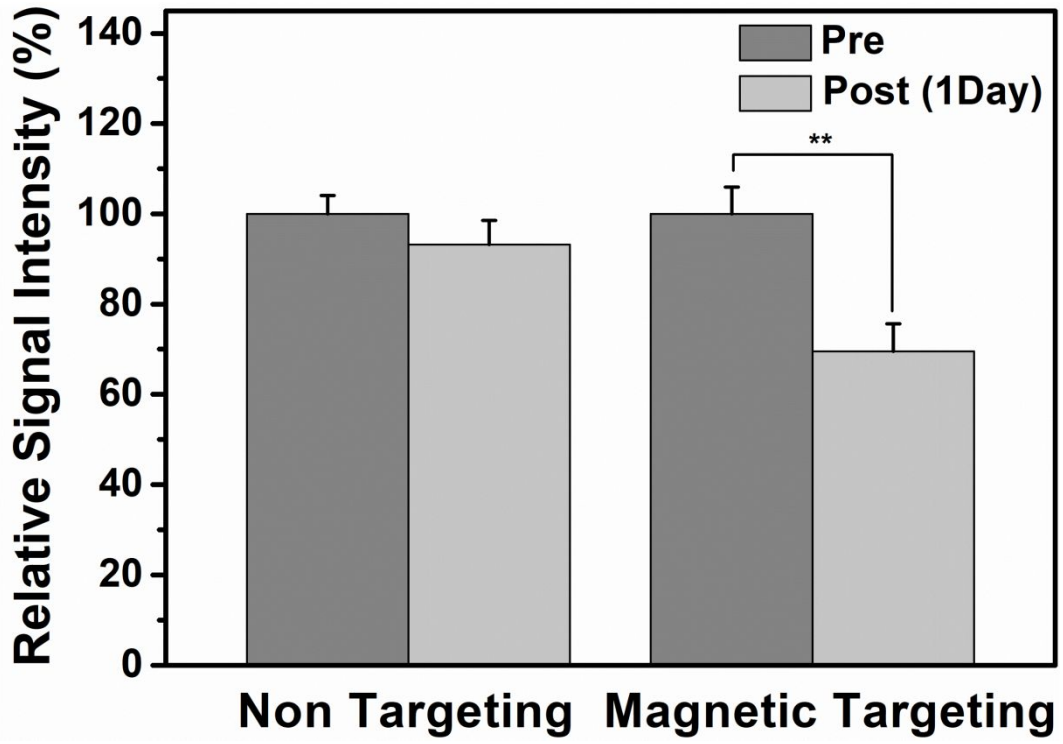

Figure S21. Intensity change of T_2-weighted MR signal before and after *i.v.* injection with or without magnetic targeting. (n = 3, mean ± *s.d.*, $^{**}p < 0.01$).

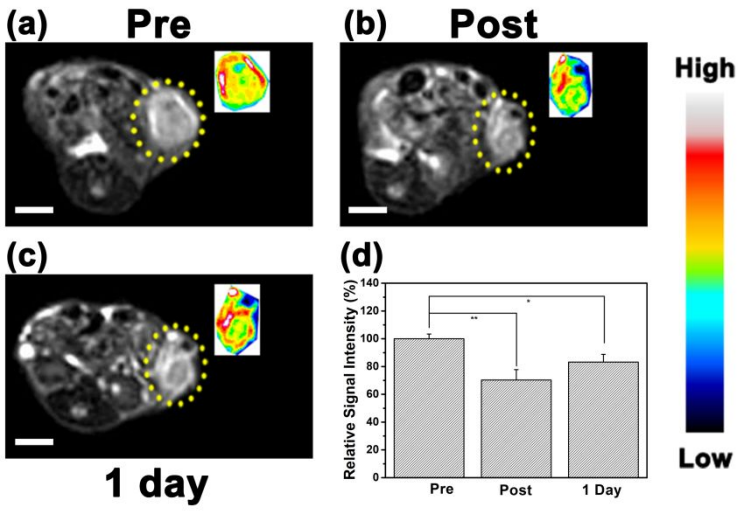

Figure S22. Representative T_2-weighted MR images of 4T1 tumor-bearing mice (**a**) before, (**b**) immediately post, and (**c**) 1 day after *i.t.* injection of PEG/Fe_5C_2@Fe_3O_4 NPs. The tumor sites are circled by a yellow dashed line. Figure at the top right corner is the pseudo-color image of the tumor site. (**d**) Intensity changes of T_2-weighted MR signal immediately or 1 day after *i.t.* injection. Scale bars are 5 mm. (n = 3, mean ± *s.d.*, *$p < 0.05$, **$p < 0.01$).

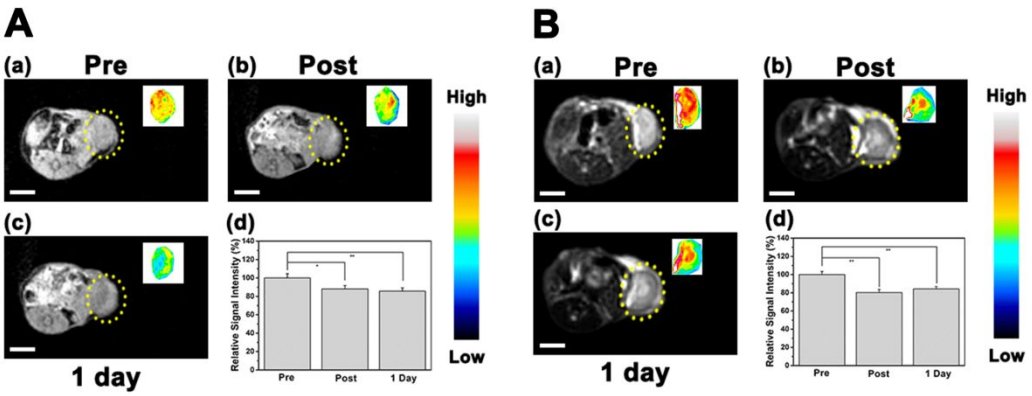

Figure S23. (**A**) Representative T_1-weighted MR images of 4T1 tumor-bearing mice (**a**) before, (**b**) immediately post, and (**c**) one day after *i.t.* injection of PEG/Fe_3O_4 NPs. The tumor sites are circled by a yellow dashed line. Figure at the top right corner is the pseudo-color image of the tumor site. (**d**) Intensity changes of T_1-weighted MR signal immediately or one day after *i.t.* injection. Scale bars are 5 mm. (n = 3, mean ± *s.d.*, *$p < 0.05$, **$p < 0.01$). (**B**) Representative T_2-weighted MR images of 4T1 tumor-bearing mice (**a**) before, (**b**) immediately post, and (**c**) 1 day after *i.t.* injection of PEG/Fe_3O_4 NPs. The tumor sites are circled by a yellow dashed line. Figure at the top right corner is the pseudo-color image of the tumor site. (**d**) Intensity changes of T_2-weighted MR signal immediately or 1 day after *i.t.* injection. Scale bars are 5 mm. (n = 3, mean ± *s.d.*, **$p < 0.01$).

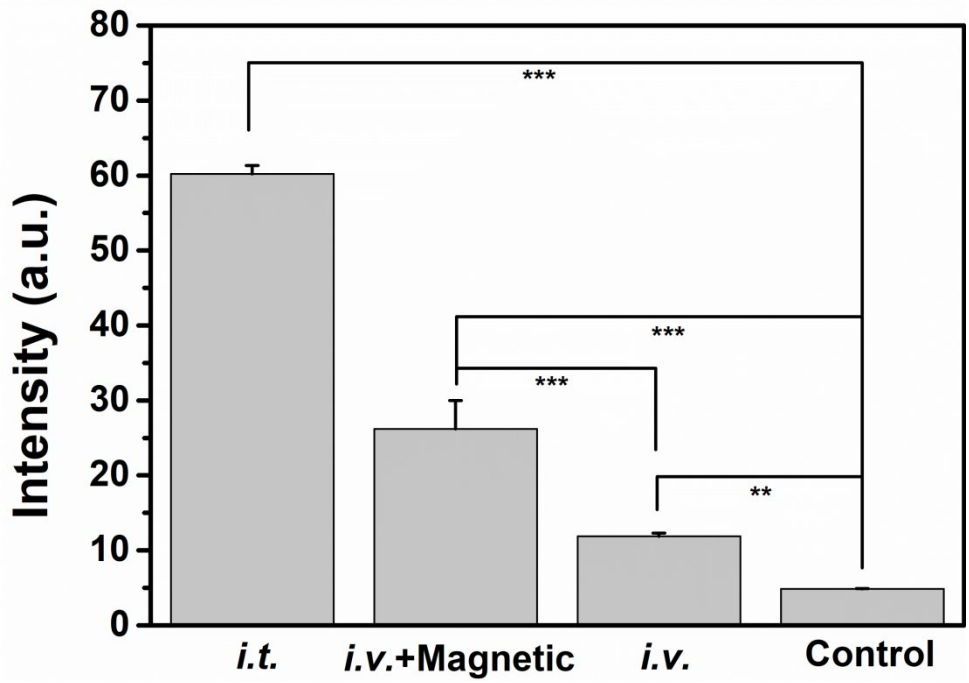

Figure S24. Fluorescence intensities of DCFH-DA labeled mice tumors by different treatments. (n = 5, mean ± *s.d.*, $^{**}p < 0.01$, and $^{***}p < 0.001$).

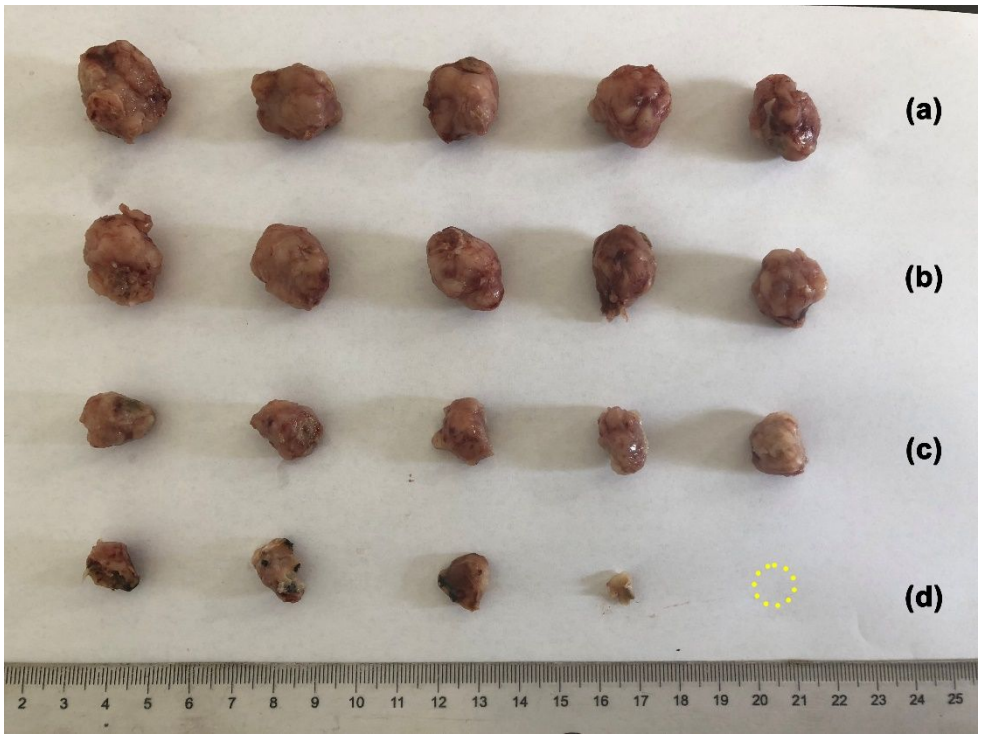

Figure S25. Photograph at day 19 of tumor from group (**a**) Control, (**b**) *i.v.* injection of PEG/Fe_5C_2@Fe_3O_4 NPs, (**c**) *i.v.* injection of PEG/Fe_5C_2@Fe_3O_4 NPs with magnetic targeting, (**d**) *i.t.* injection of PEG/Fe_5C_2@Fe_3O_4 NPs. One tumor in group (**d**) was completely inhibited, and showed by a dash circle. The initial tumor sizes were about 100 mm^3.

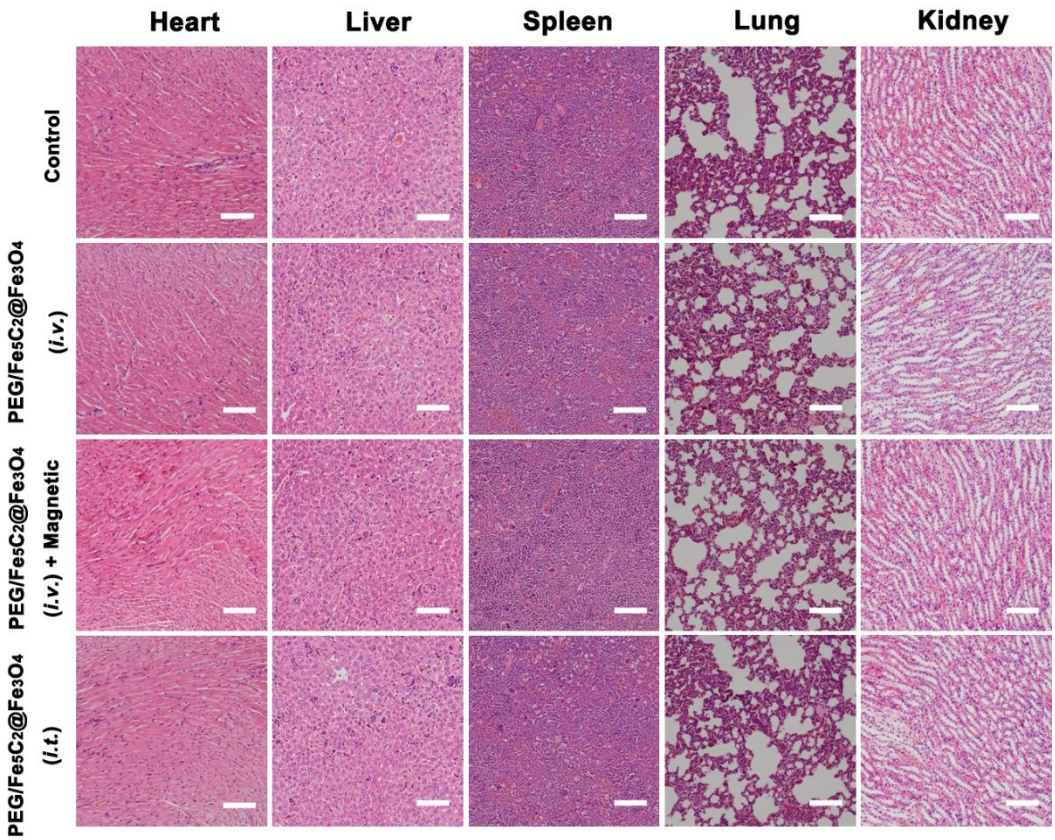

Figure S26. H&E stained images of major organs collected from different groups of mice. Scale bars are 500 μm.

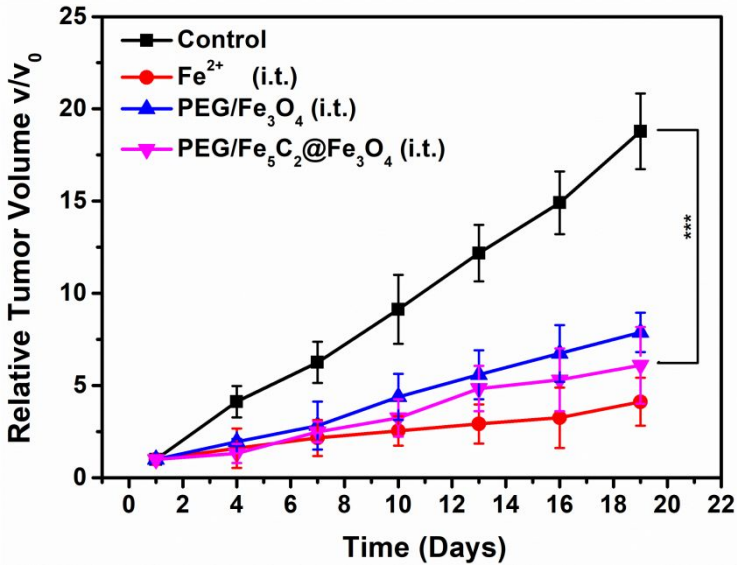

Figure S27. Time course change in the relative tumor volume after different treatments. The initial tumor sizes were about 150 mm^3. (n = 5, mean ± *s.d.*, ***p < 0.001).

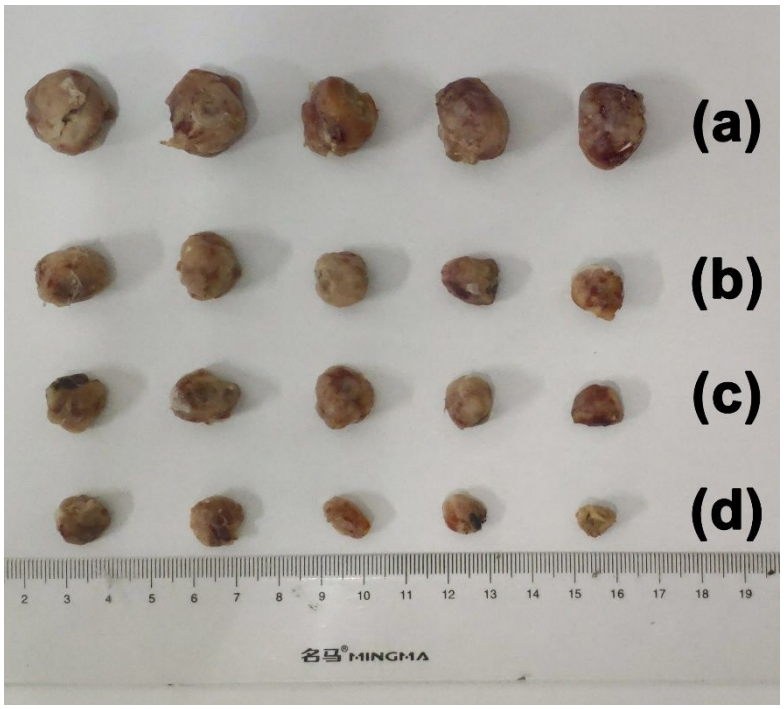

Figure S28. Photographs at day 19 of tumor from group (**a**) Control, (**b**) *i.t.* injection of PEG/Fe_3O_4 NPs, (**c**) *i.t.* injection of PEG/Fe_5C_2@Fe_3O_4 NPs, (**d**) *i.t.* injection of Fe^{2+}. The initial tumor sizes were about 150 mm^3.

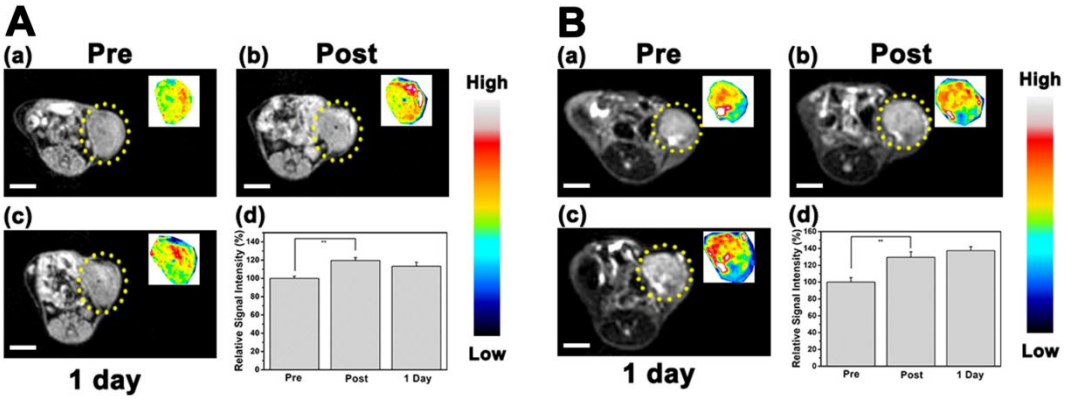

Figure S29. (**A**) Representative T_1-weighted MR images of 4T1 tumor-bearing mice (**a**) before, (**b**) immediately post, and (**c**) one day after *i.t.* injection of Fe^{2+} ions ($FeCl_2$). The tumor sites are circled by a yellow dashed line. Figure at the top right corner is the pseudo-color image of the tumor site. (**d**) Intensity changes of T_1-weighted MR signal immediately or one day after *i.t.* injection. Scale bars are 5 mm. (n = 3, mean ± *s.d.*, $^{**}p < 0.01$) (**B**) Representative T_2-weighted MR images of 4T1 tumor-bearing mice (**a**) before, (**b**) immediately post, and (**c**) 1 day after *i.t.* injection of Fe^{2+} ions ($FeCl_2$). The tumor sites are circled by a yellow dashed line. Figure at the top right corner is the pseudo-color image of the tumor site. (**d**) Intensity changes of T_2-weighted MR signal immediately or 1 day after *i.t.* injection. Scale bars are 5 mm. (n = 3, mean ± *s.d.*, $^{**}p < 0.01$).

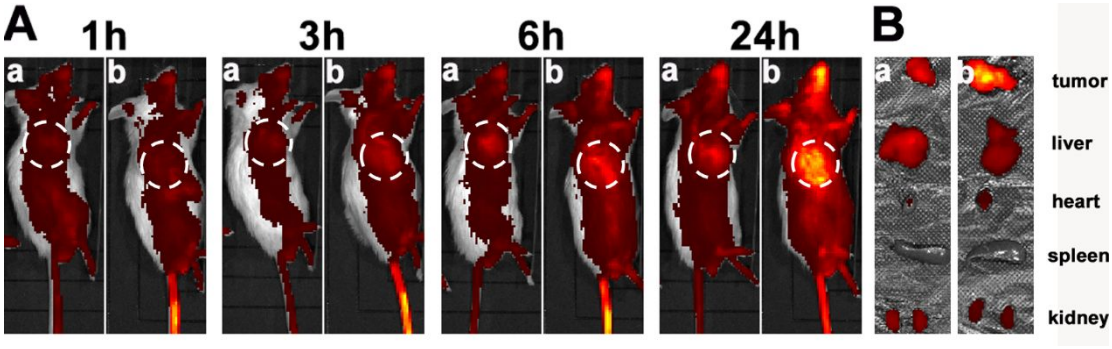

Figure S30. (**A**) *In vivo* NIR imaging of tumor-bearing mice intravenous injected with IR783-labeled PEG/Fe_5C_2@Fe_3O_4 NPs at 1, 3, 6, and 24 h post-injection (**a**: PEG/Fe_5C_2@Fe_3O_4-IR783; **b**: PEG/Fe_5C_2@Fe_3O_4-IR783 + Magnet. Circled area: tumor site). (**B**) NIR imaging of various tissues at 24 h post-injection (**a**: PEG/Fe_5C_2@Fe_3O_4-IR783; **b**: PEG/Fe_5C_2@Fe_3O_4-IR783 + Magnet).

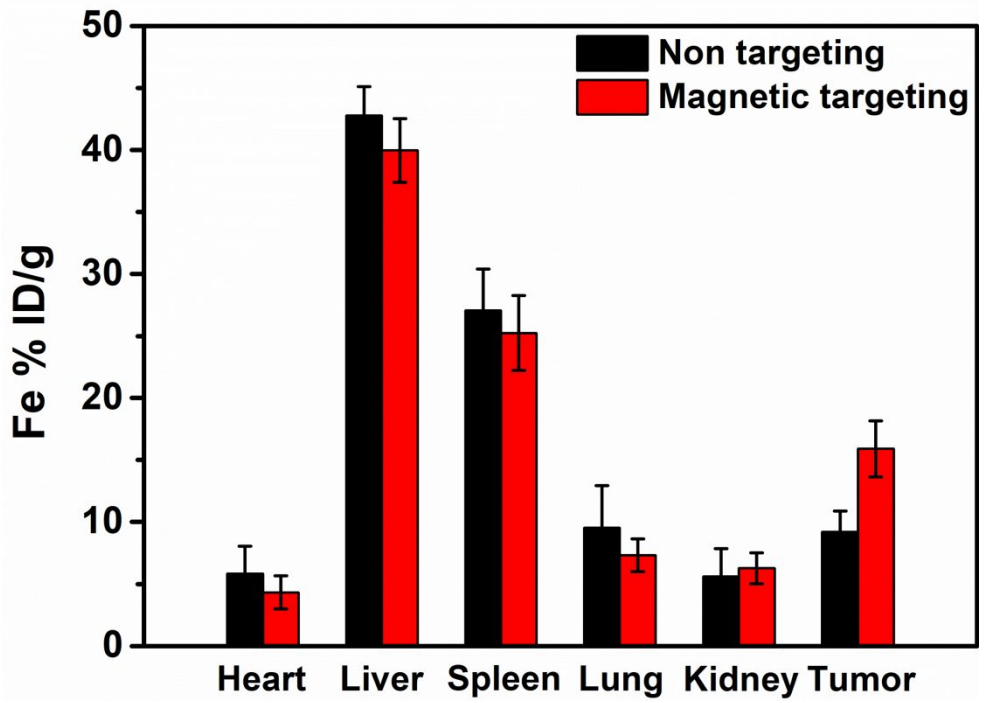

Figure S31. Biodistribution of Fe (% administrated dose (ID) of Fe per gram of tissues) in main tissues and tumors after *i.v.* administrations with or without magnetic targeting for 24 h.