

Electronic Supplementary Material

Smart magnetic nanosystem sequentially extracellular and intracellular release proteins for cancer therapy

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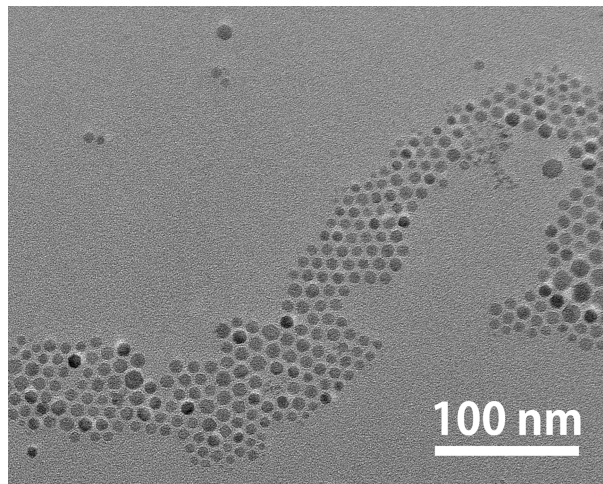


Figure S1. TEM image of IONPs

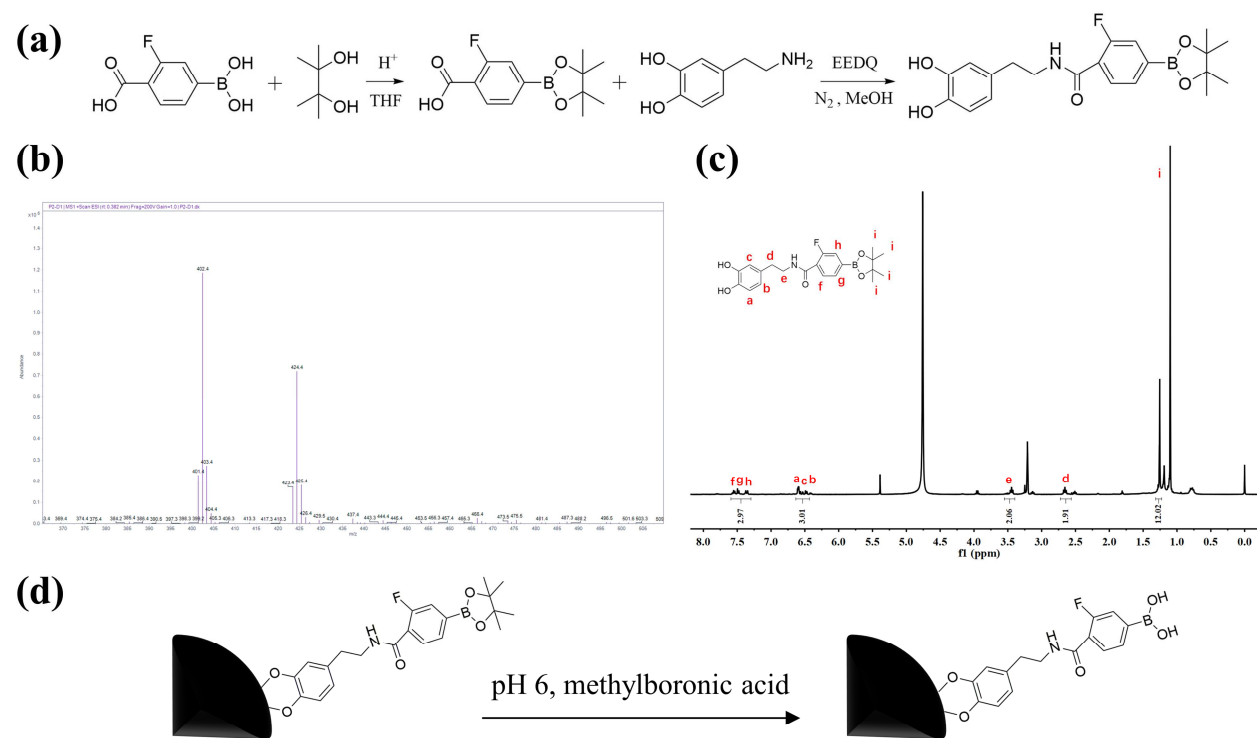


Figure S2. Characterization of the ligand. (a) Synthetic procedures of protected DPA-FPBA; (b) Mass spectrum of protected DPA-FPBA; (c) ^1H -NMR spectrum of protected DPA-FPBA. (d) The process of removing pinacol from the protected DPA-FPBA.

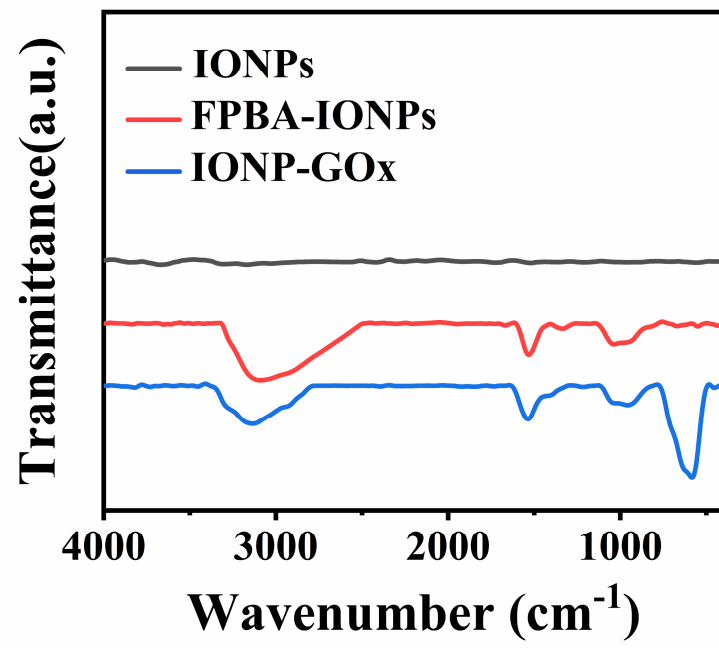


Figure S3. FT-IR spectra of IONPs, FPBA-IONPs and IONP-GOx.

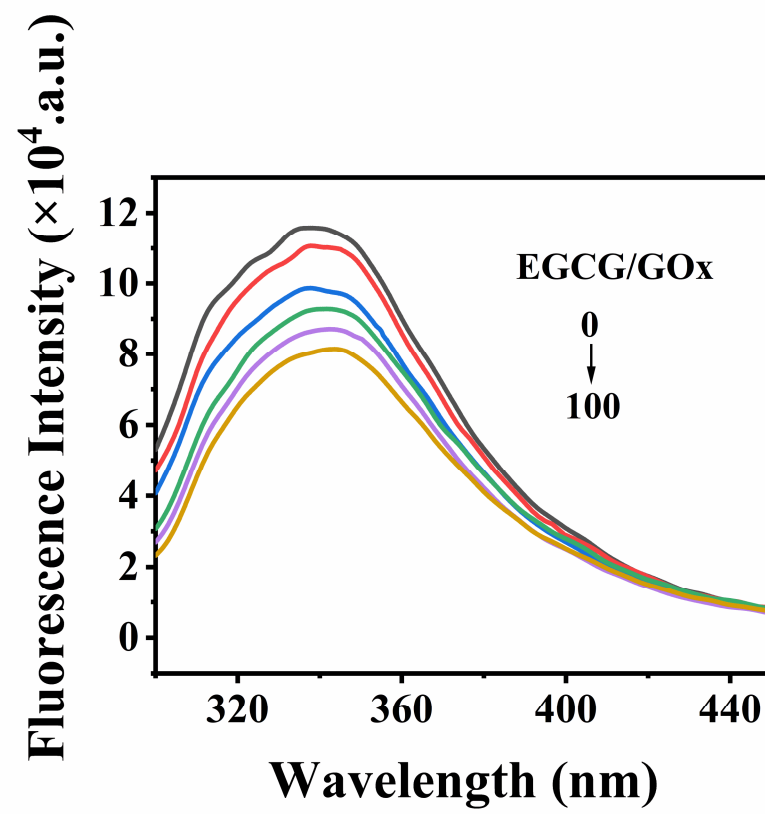


Figure S4. Fluorescence change of GOx in the presence of EGCG. The molar ratios of EGCG/GOx were 0:1, 10:1, 30:1, 50:1, 70:1 and 100:1.

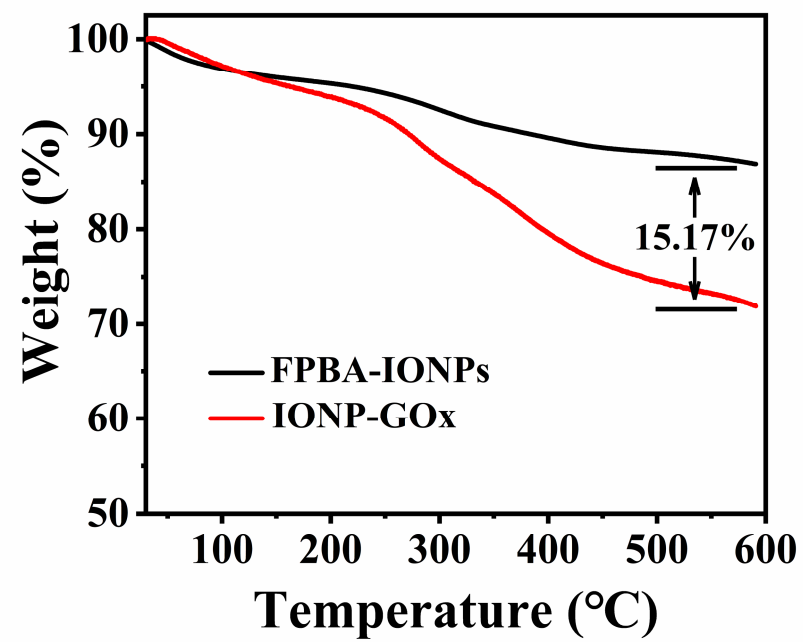


Figure S5. TGA curves of FPBA-IONPs and IONP-GOx in N₂.

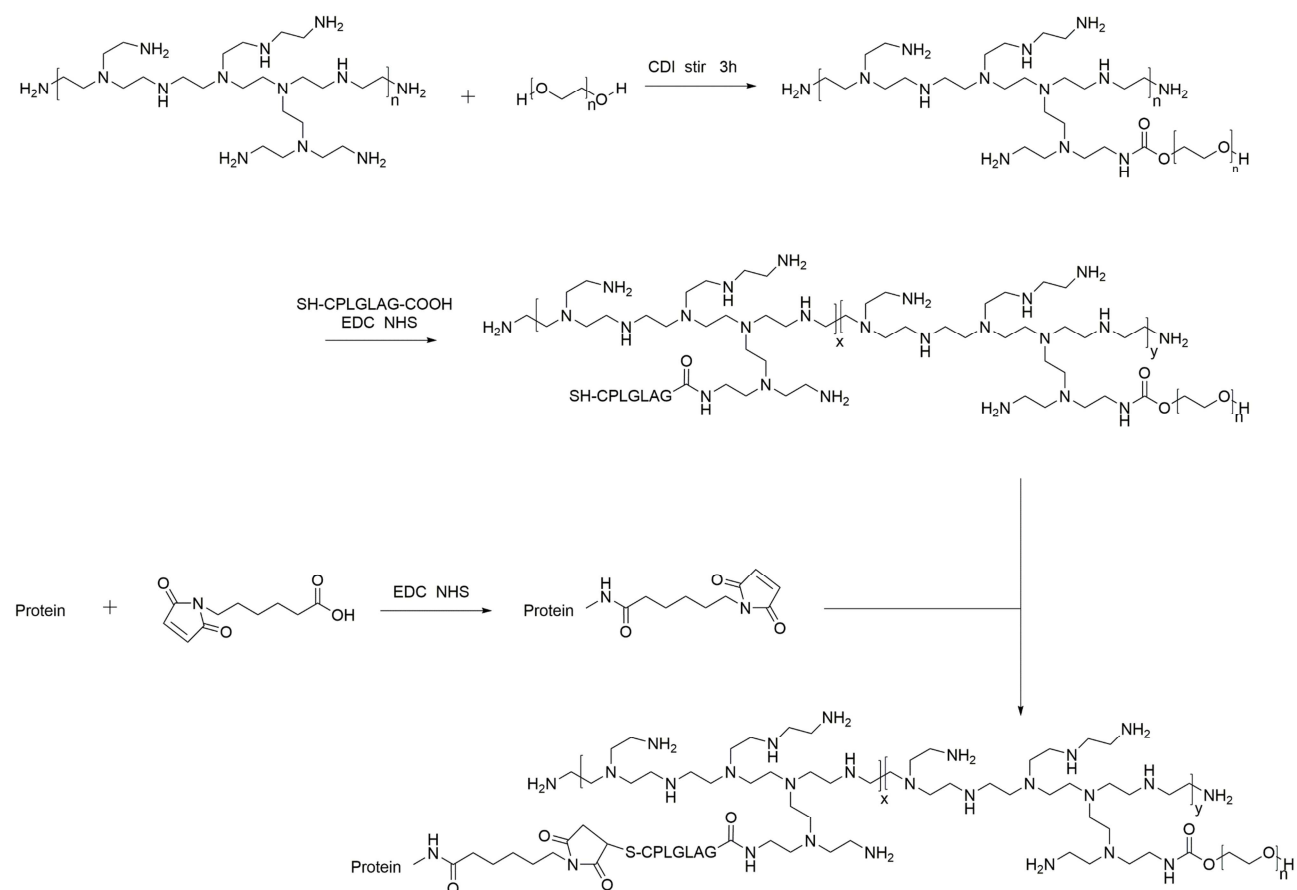


Figure S6. Synthesis of PEI-PEG-TRAIL.

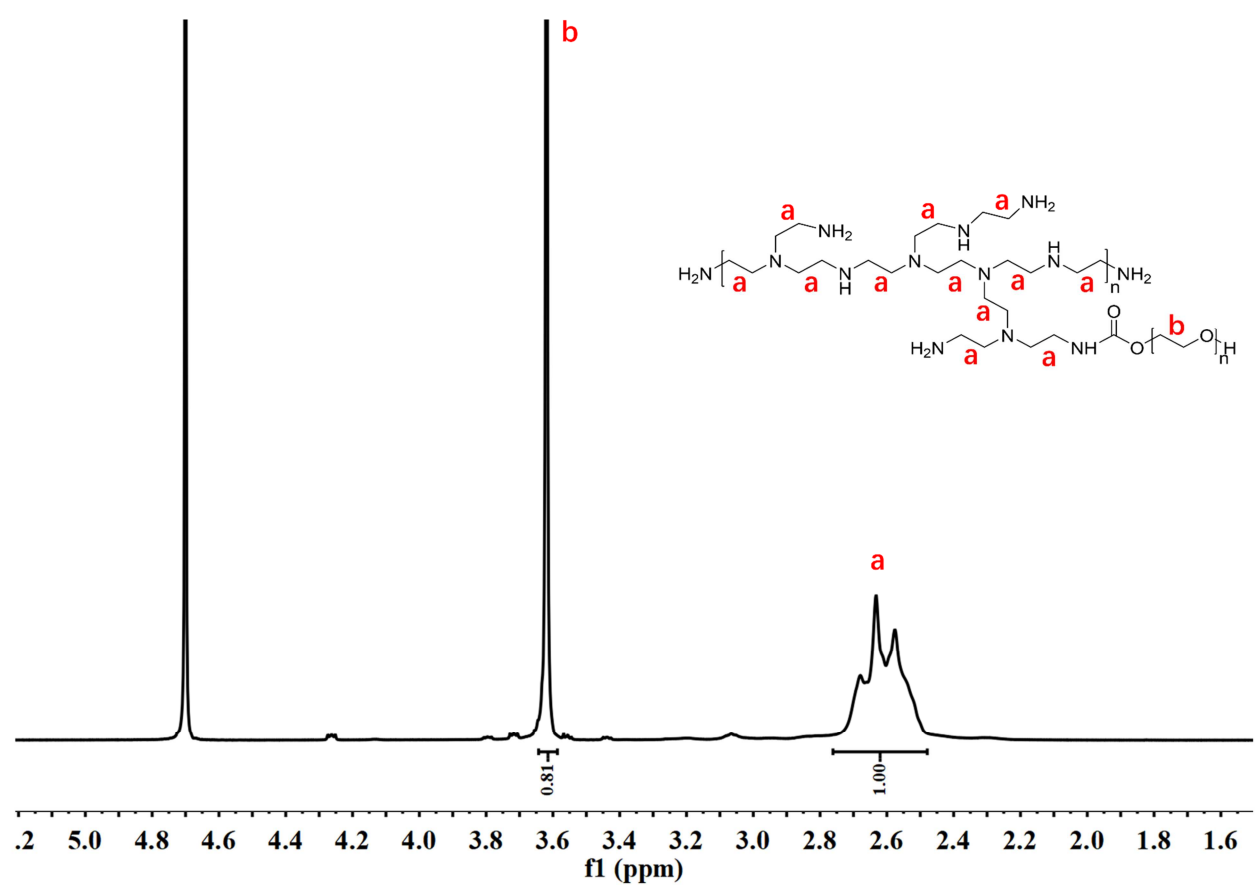


Figure S7. ^1H -NMR spectrum of PEI-PEG.

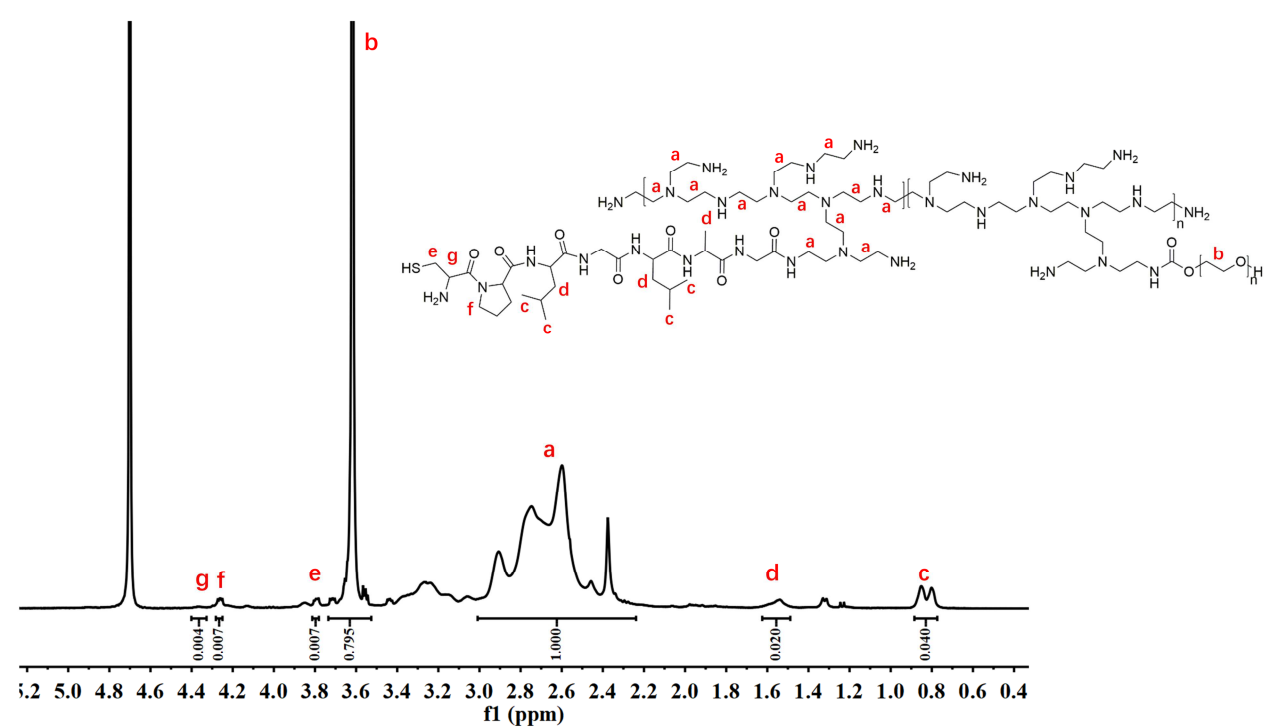


Figure S8. ^1H -NMR spectrum of PEI-PEG-CPLGLAG.

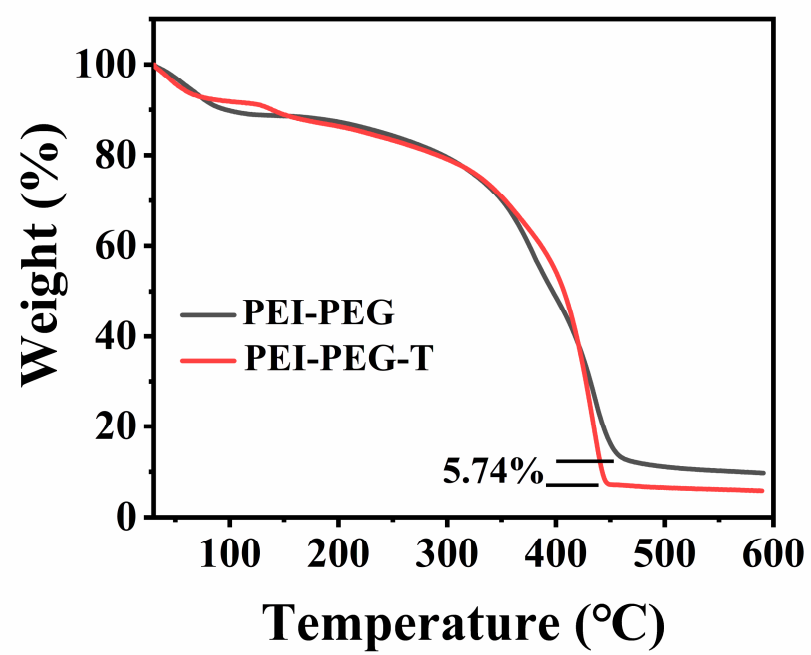


Figure S9. TGA curves of PEI-PEG and PEI-PEG-TRAIL in N₂.

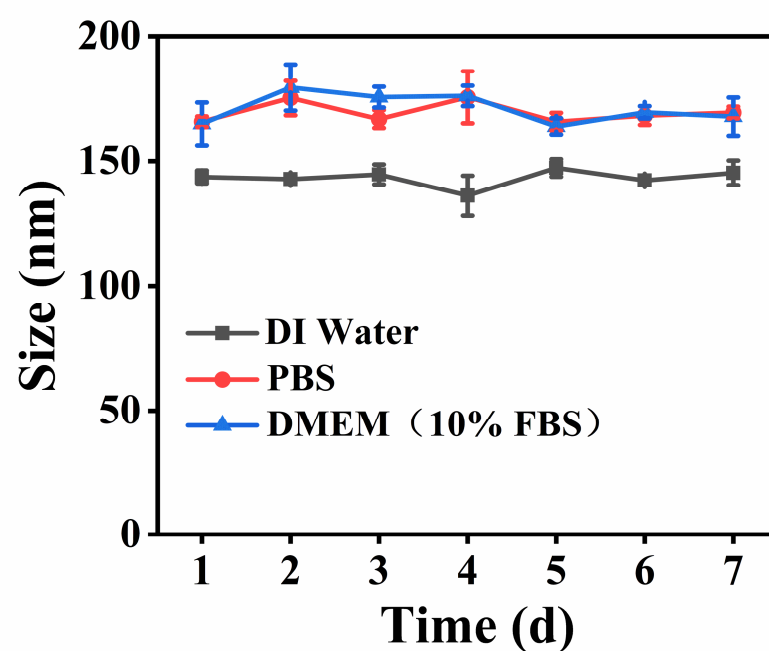


Figure S10. Hydrodynamic diameters of PEI-PEG-TRAIL@IONP-GOx in DI water, PBS, and DMEM (10% FBS) within 7 days. Data were represented as mean \pm SD (n = 3).

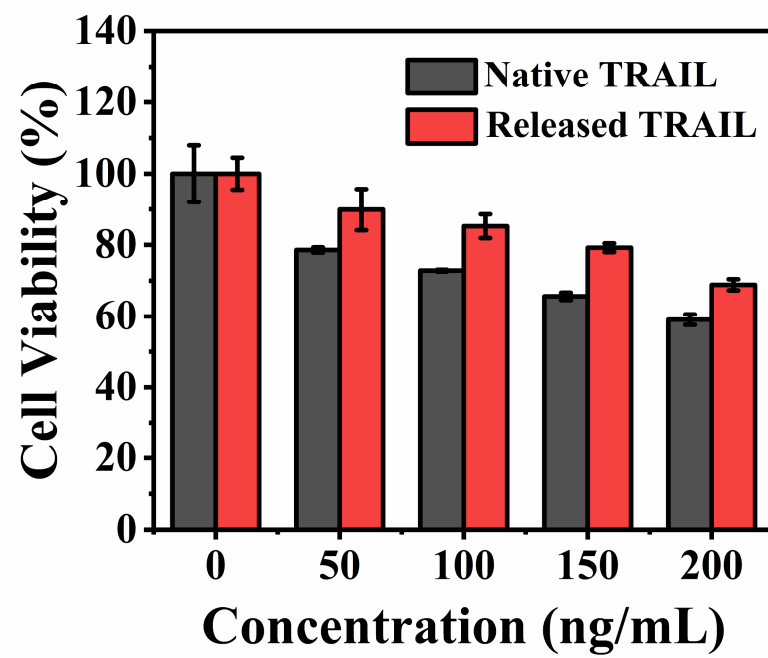


Figure S11. Cell cytotoxicity of standard native TRAIL solution and TRAIL released from PEI-PEG-TRAIL@IONP-GOx on HeLa cells for 24 h. Data were represented as mean \pm SD (n = 3).

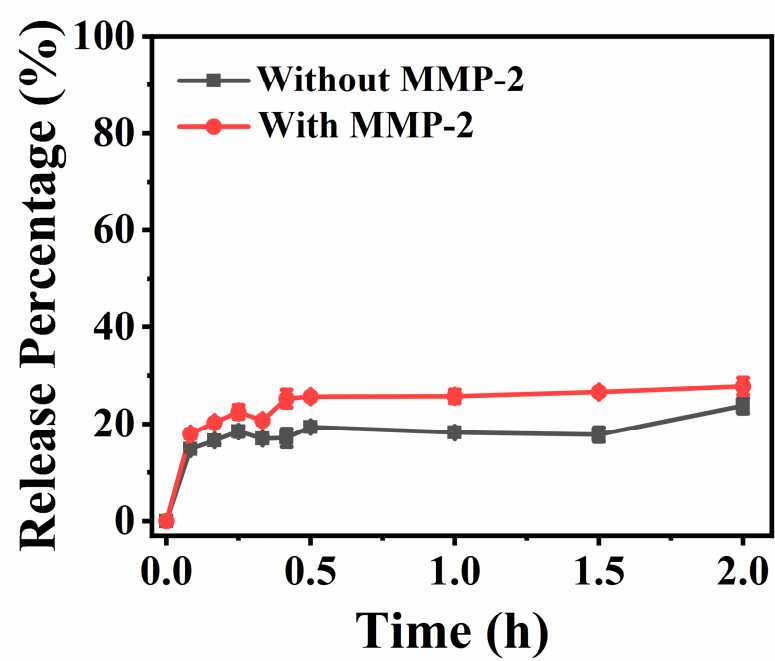


Figure S12. Release curves of GOx from PEI-PEG-TRAIL@IONP-GOx with or without type IV collagenase (20 μ g/mL). Data were represented as mean \pm SD (n = 3).

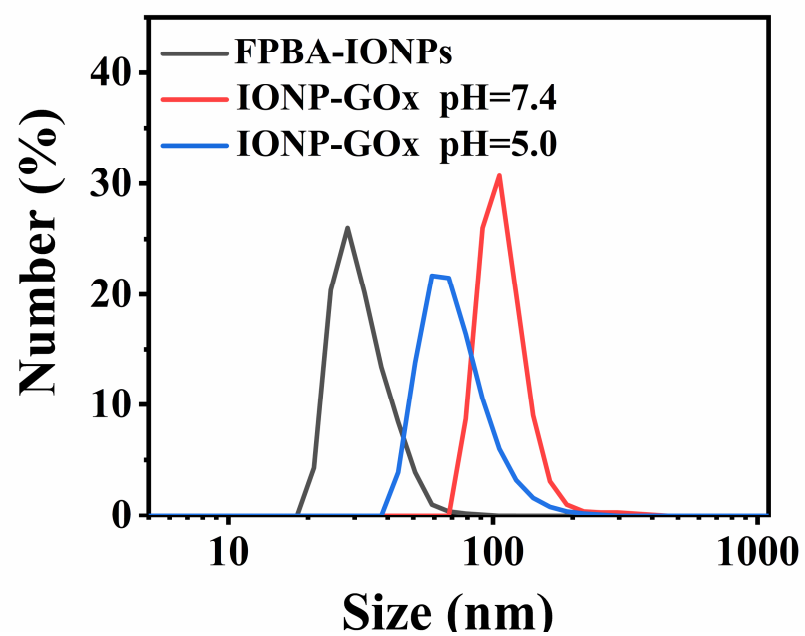


Figure S13. Hydrodynamic diameters of IONP-GOx after incubation at pH 7.4 and pH 5.5. Data were represented as mean \pm SD (n = 3).

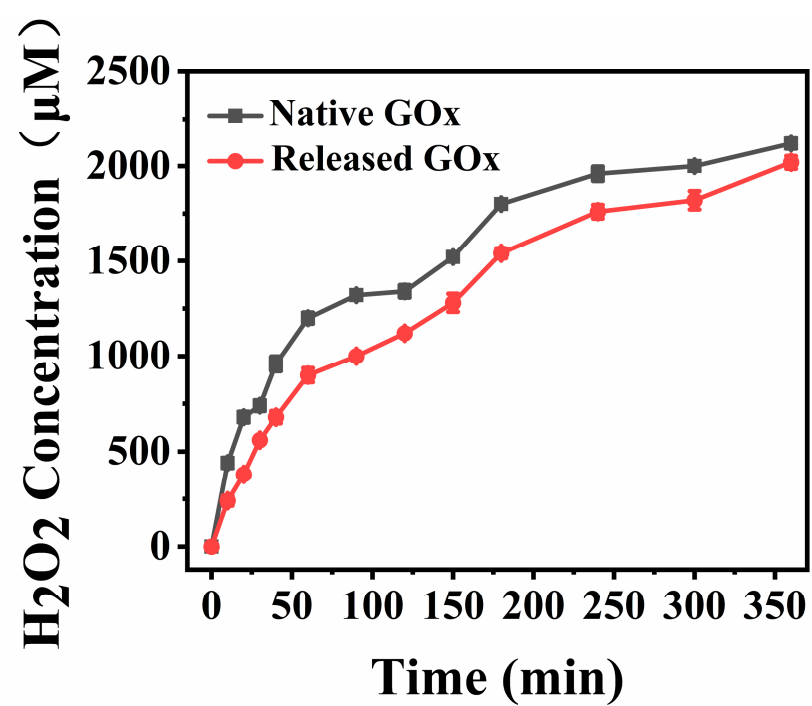


Figure S14. H₂O₂ generation curves of standard native GOx solution and GOx released from IONP-GOx with the addition of glucose ([GOx] = 2 μ g/mL, [glucose] = 0.6 mg/mL). Data were represented as mean \pm SD (n = 3).

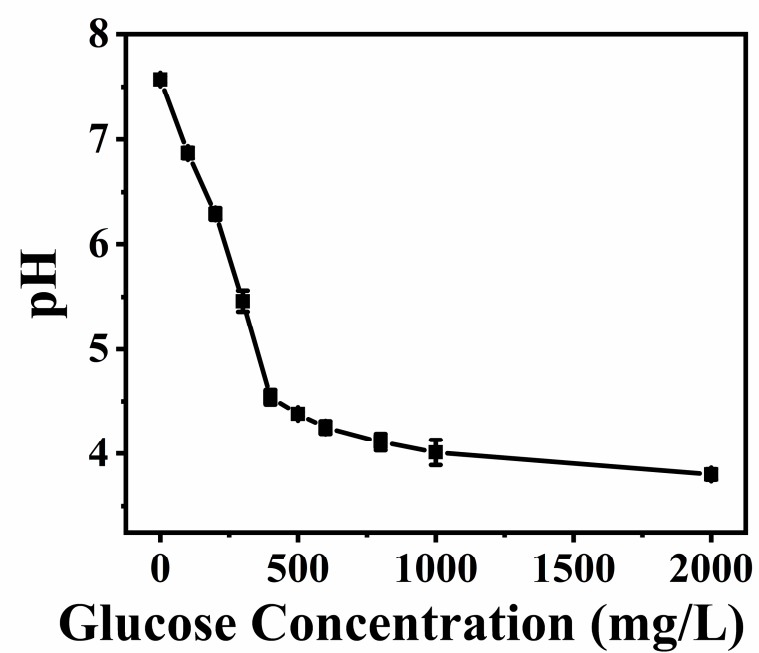


Figure S15. Glucose-dependent pH changes of the mixture of FPBA-IONPs and GOx ([GOx] = 2 $\mu\text{g/mL}$). Data were represented as mean \pm SD (n = 3).

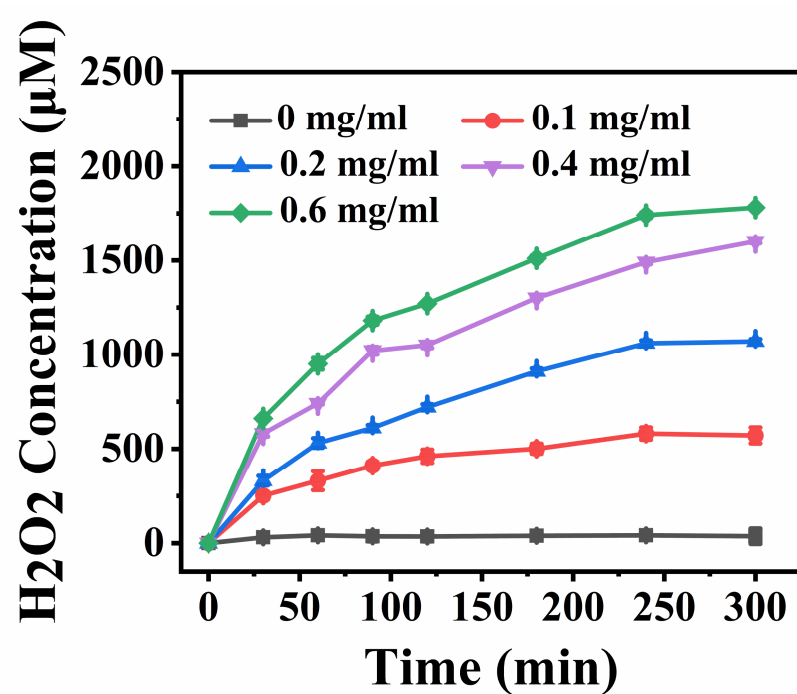


Figure S16. Glucose-dependent H_2O_2 concentration changes of the mixture of FPBA-IONPs and GOx ([GOx] = 2 $\mu\text{g/mL}$). Data were represented as mean \pm SD (n = 3).

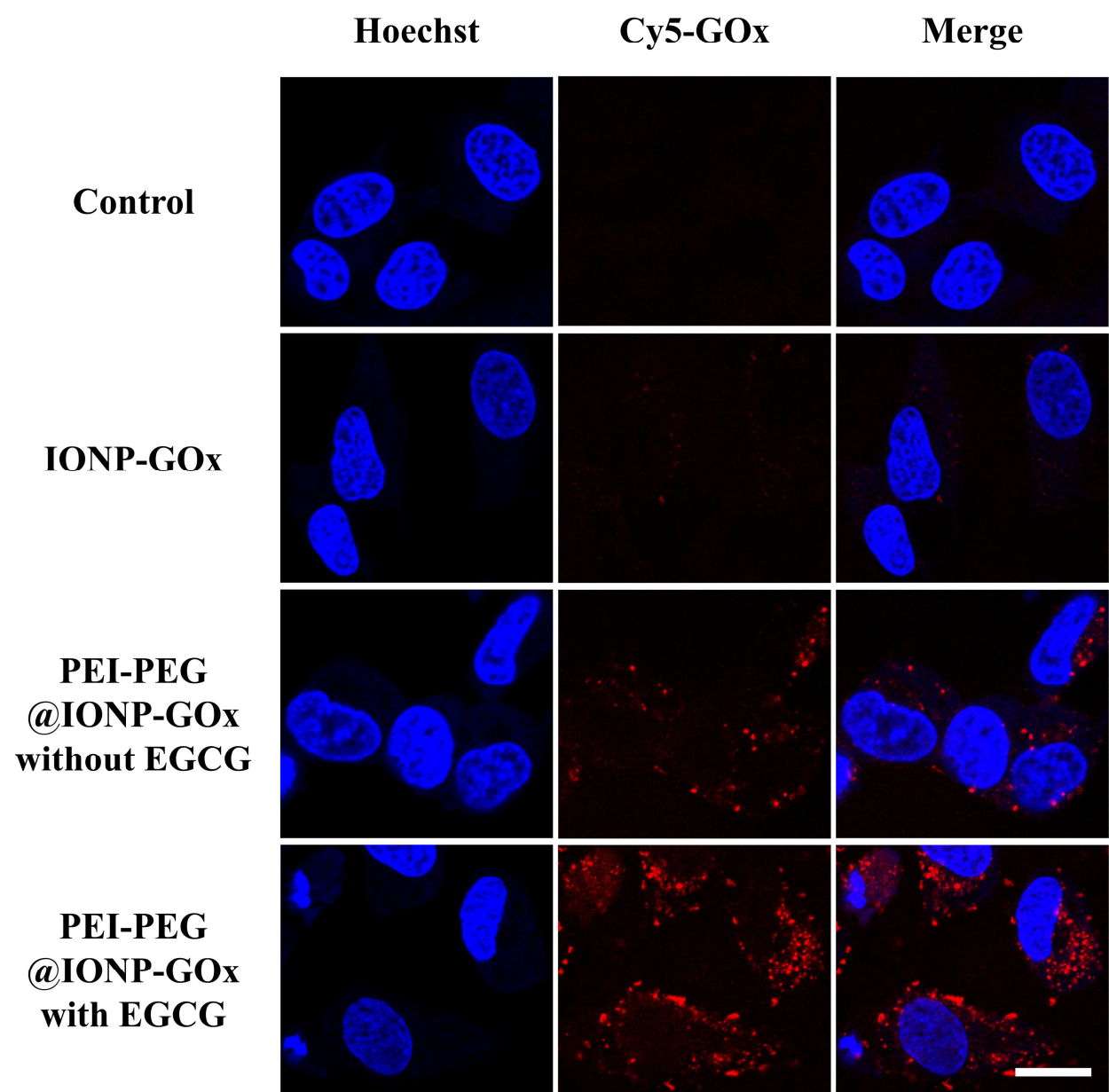


Figure S17. CLSM images of Hela cells after incubation with different formulations for 6 h. Scale bar: 20 μm .

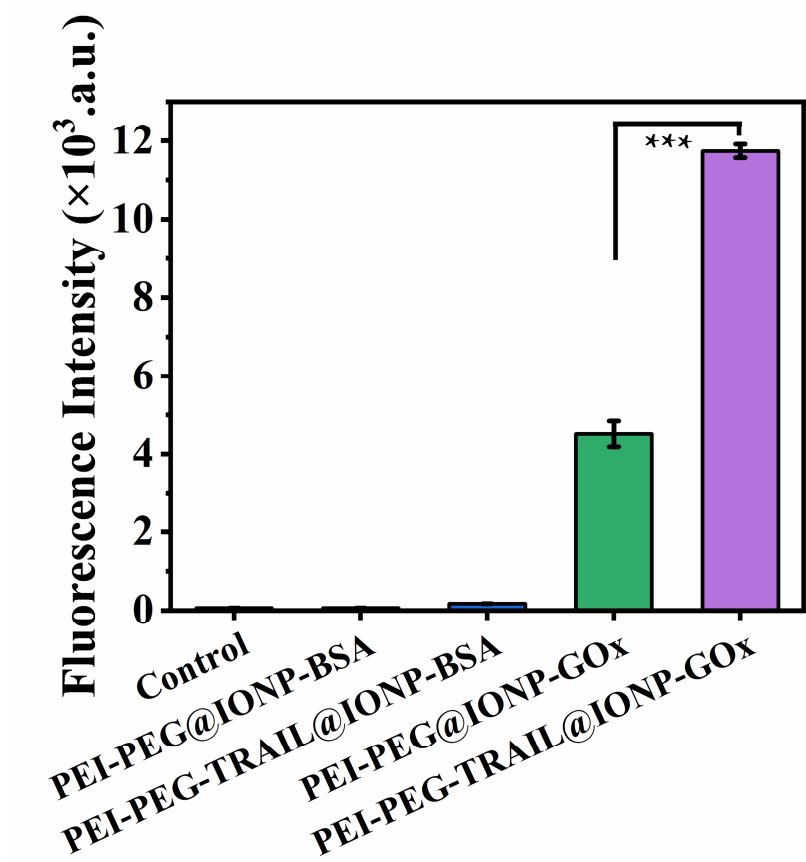


Figure S18. Semi-quantitative analysis of ROS generation from the fluorescence images. Data were represented as mean \pm SD (n = 3). ***P < 0.001.

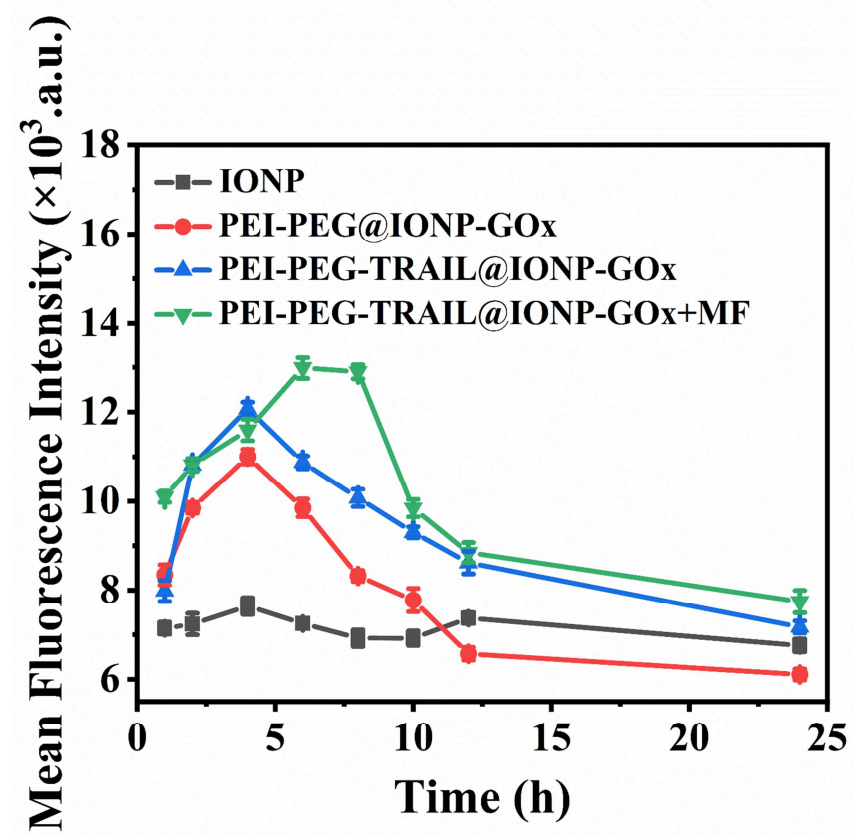


Figure S19. Mean fluorescence intensity of the tumor tissues after intravenous injection of different formulations at various time points. Data were represented as mean \pm SD (n = 3).

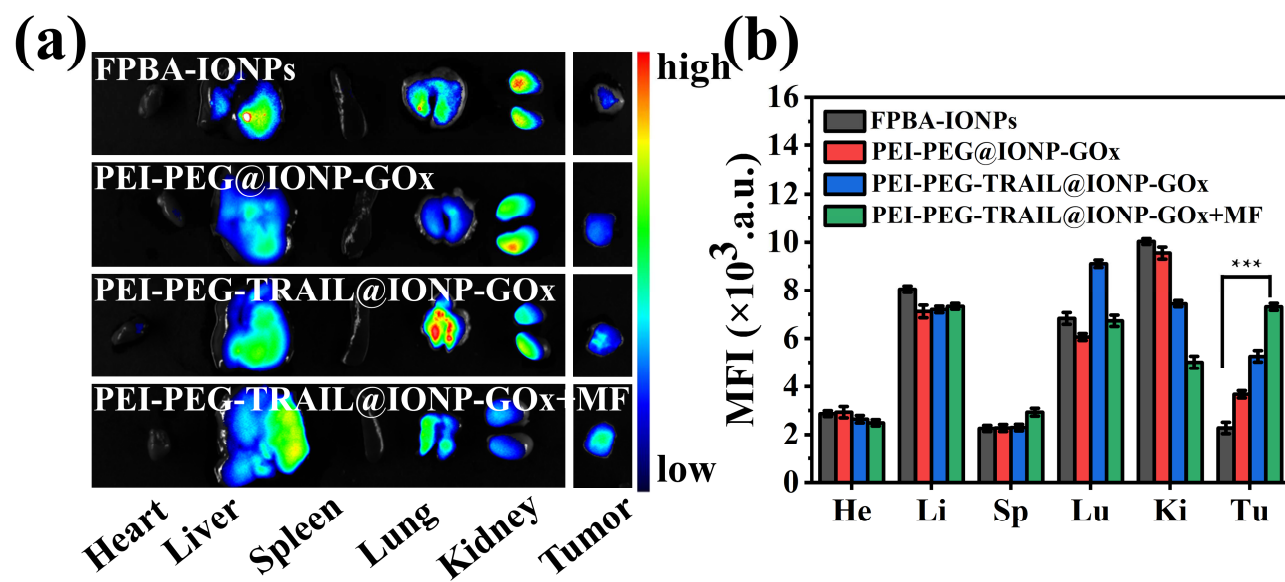


Figure S20. *Ex vivo* fluorescence images of major organs and semi-quantitative analysis. (a) *Ex vivo* fluorescence images of major organs and tumors at 4 h after injection of different formulations. (b) The semi-quantitative analysis of fluorescence signal of major organs and tumors after injection of different formulations. Data were represented as mean \pm SD (n = 3). ***P < 0.001.

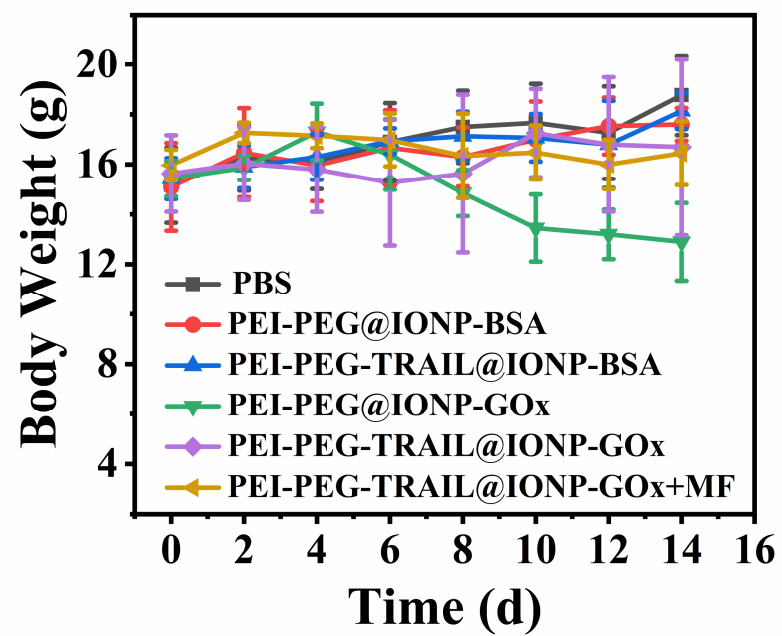


Figure S21. Body weight during 14 days treatment. Data were represented as mean \pm SD (n = 3).

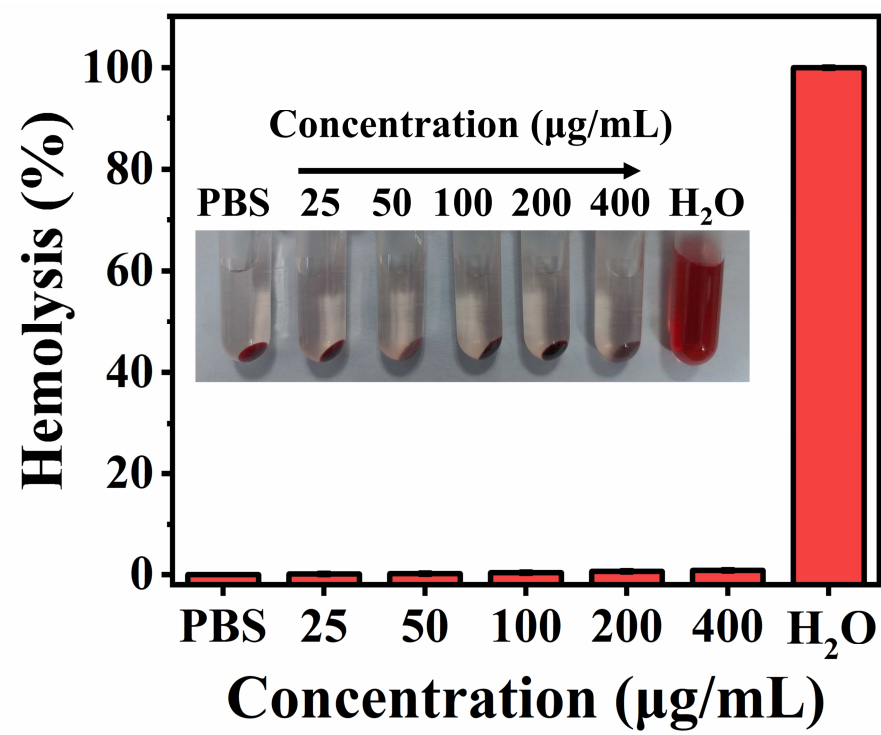


Figure S22. Hemolysis analysis of PEI-PEG-TRAIL@IONP-GOx suspension at various concentrations. Data were represented as mean \pm SD (n = 3).

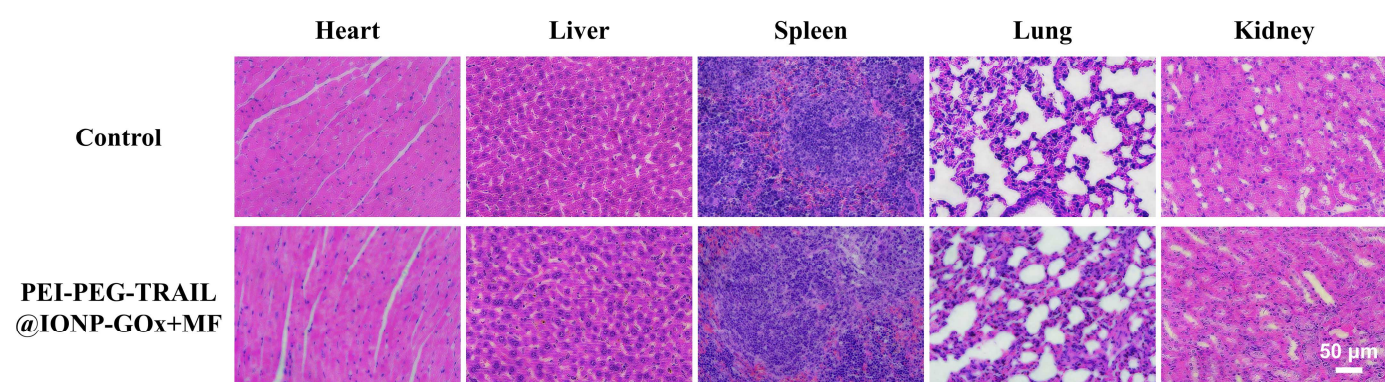


Figure S23. H&E staining of major organs (heart, liver, spleen, lung, kidney) for healthy and PEI-PEG-TRAIL@IONP-GOx+MF treated mice.

Table S1. Particle size change of IONP-GOx at pH 7.4, 6.5, 5.5.

Molar ratio of DPA and DPA-FPBA	pH 7.4	pH 6.5	pH 5.5
1	212/-22	190/-16.9	190/-16.9
21/4	194/-16.3	78.8/-15.3	68/-13.37
18/7	144/-16.7	190/-15.3	63.4/-17.83
7/13	267/-22	254/-22.4	262/-20.6
0	104/-27	N.A.	N.A.