Supporting Information

Bioinspired nanocatalytic tumor therapy by simultaneous reactive oxygen species generation enhancement and glutamine pathway-mediated glutathione depletion

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Supplementary Methods

Materials

Sodium salicylate (NaSal), triethanolamine (TEA), tetraethyl orthosilicate (TEOS), cetyltrimethylammonium bromide (CTAB), (3-Aminopropyl) triethoxysilane, iron chloride ($FeCl_3 \cdot 6H_2O$), oleyl alcohol, sodium oleate, $HAuCl_4 \cdot 4H_2O$, diphenyl ether, sodium phosphate dibasic (Na_2HPO_4), and acetic acid were purchased from Macklin Biochemical Co., Ltd (Shanghai, Chain). Acetone, n-hexane and ethanol were purchased from Fuchen Chemical Reagent Co., Ltd (Tianjin, China). 3,3',5,5'-tetramethylbenzidine (TMB) was obtained from Aladdin Co., Ltd (Shanghai, China). Hydrochloric acid (HCl), glucose, and hydrogen peroxide (H_2O_2) were ordered from Sinopharm Chemical Reagent Co., Ltd (Shanghai, China). Fluorescein isothiocyanate (FITC) and Methoxy PEG-thiol (mPEG-SH, Mw = 5000) were received from Xi'an Ruixi Biological Technology Co., Ltd (xi'an, Chain). Dimethyl sulfoxide (DMSO) was from Merck Co., Inc. (Germany). All chemicals were used as received without further purification.

Cell Culture

Murine breast cancer cells 4T1, human pulmonary carcinoma cells A549, human umbilical vein endothelial (HUVEC) cells and rat myoblast L6 cells were obtained from Cell Resource Center, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences (Shanghai, China) and 4T1 cells were used as the model cells in this work. All cells were maintained in high glucose DMEM medium with FBS (10%, v/v), penicillin/streptomycin (1%, v/v) and incubated under 37 °C with 5% CO_2 in a humidified incubator.

Supplementary Figures

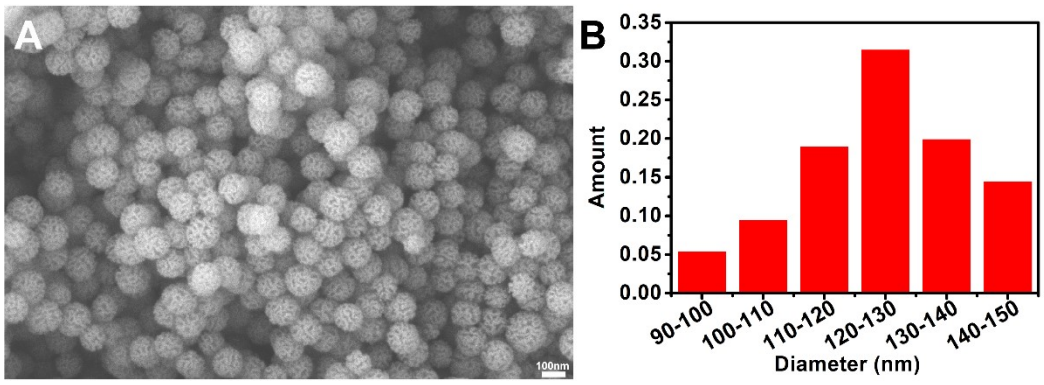


Fig. S1. (A) SEM image and (B) size distribution histogram of DMSN.

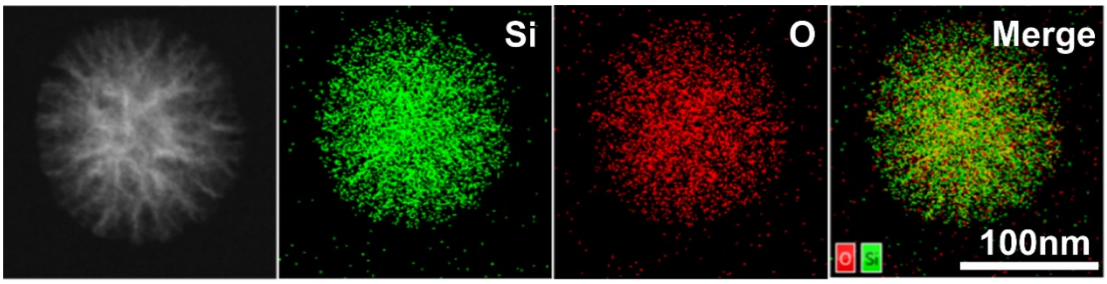


Fig. S2. Dark-field STEM image of DMSN NPs and corresponding element mappings for elements of O, Si and merge, respectively.

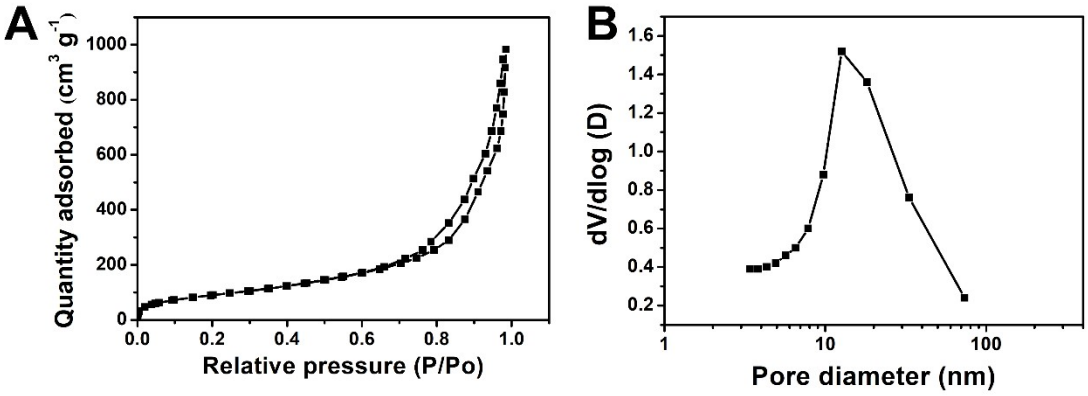


Fig. S3. (A) N_2 sorption isotherms and (B) pore size distributions of DMSN.

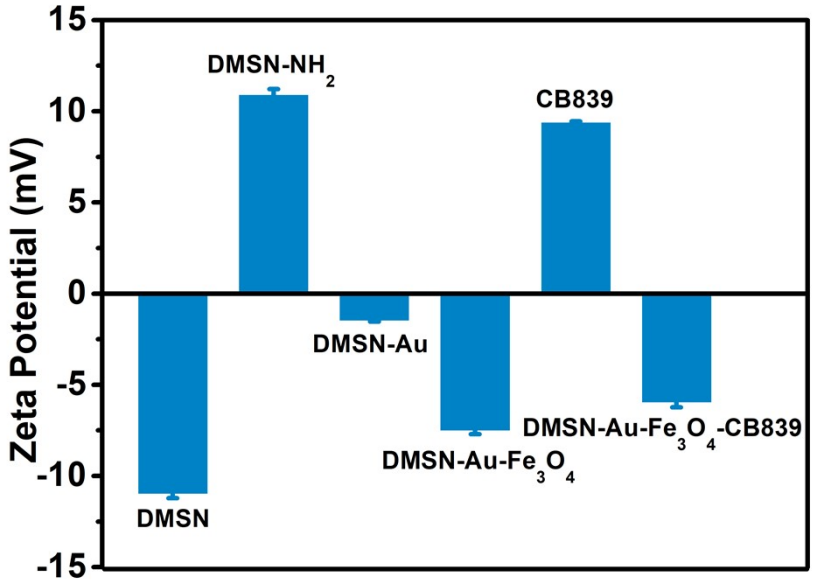


Fig. S4. Zeta potentials of samples.

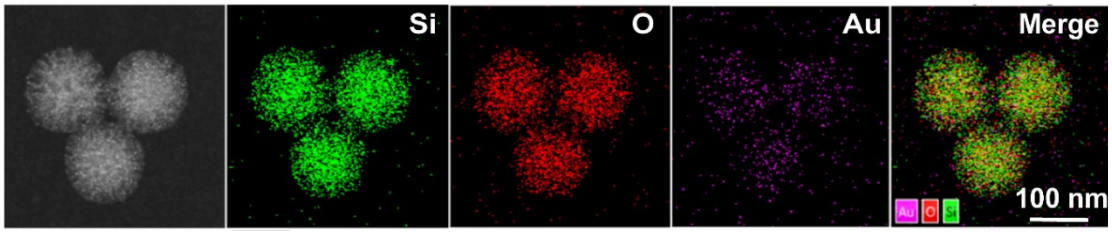


Fig. S5. Dark-field STEM image of DMSN-Au NPs and corresponding element mappings for elements of O, Si, Au and merge, respectively.

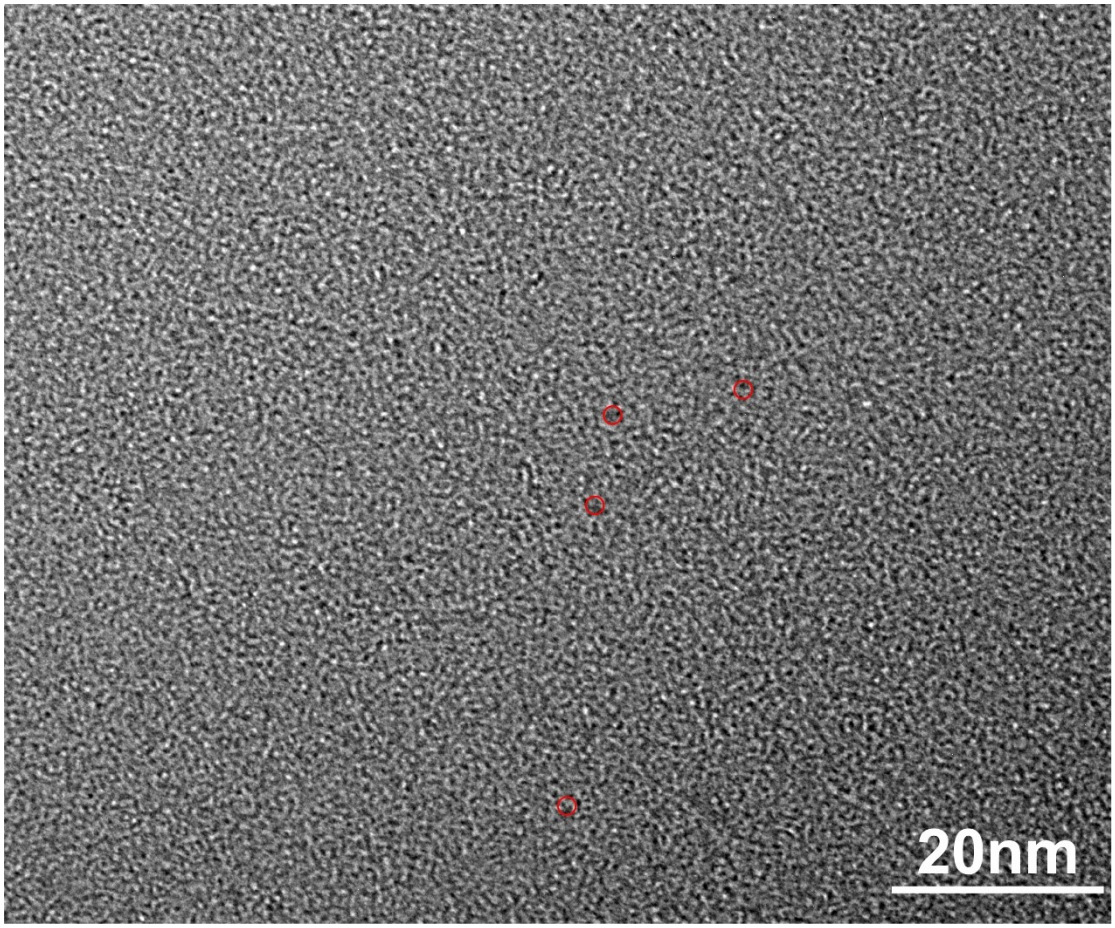


Fig. S6. TEM image of monodispersed ultrasmall Fe_3O_4 NPs.

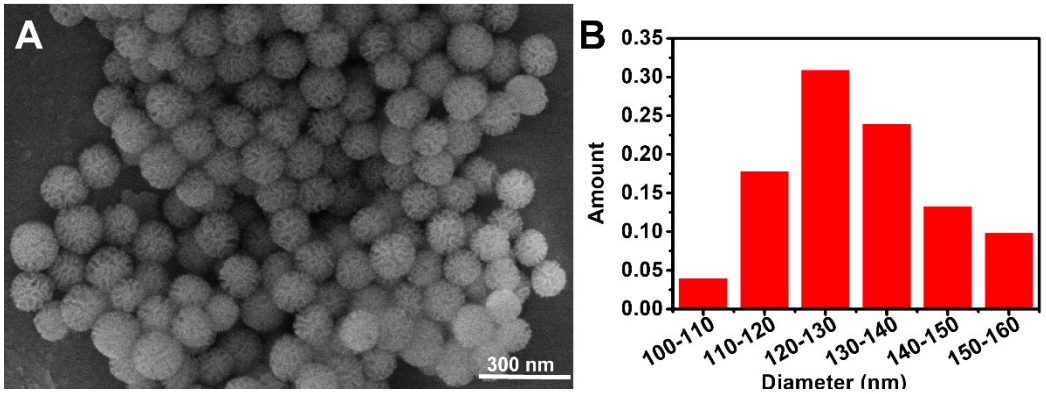


Fig. S7. (A) SEM image and (B) size distribution histogram of DMSN-Au-Fe_3O_4.

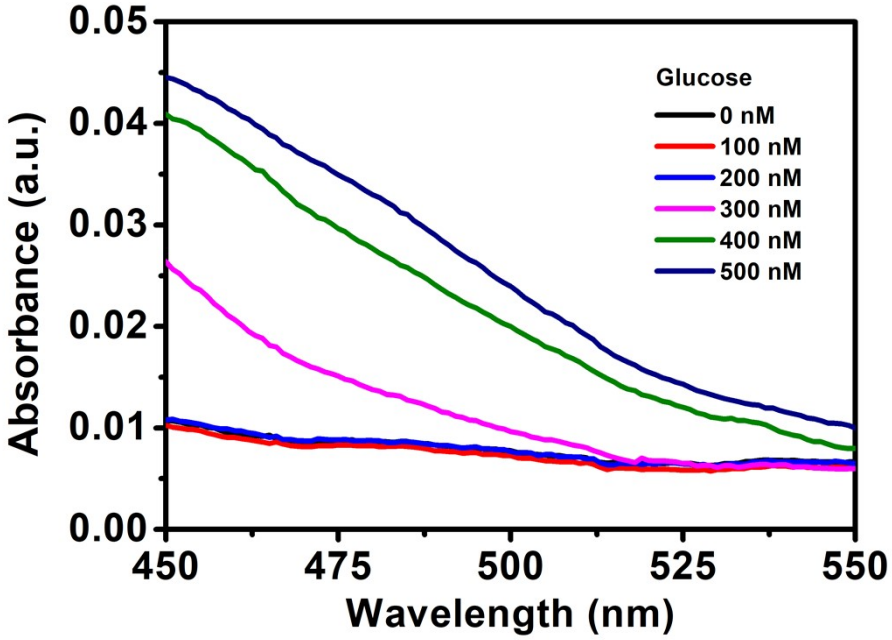


Fig. S8. UV–vis absorption spectra of DMSN-Au-Fe_3O_4 after incubation with glucose at varied concentrations (0, 100, 200, 300, 400, 500 × 10^{-3} M) for 1 h.

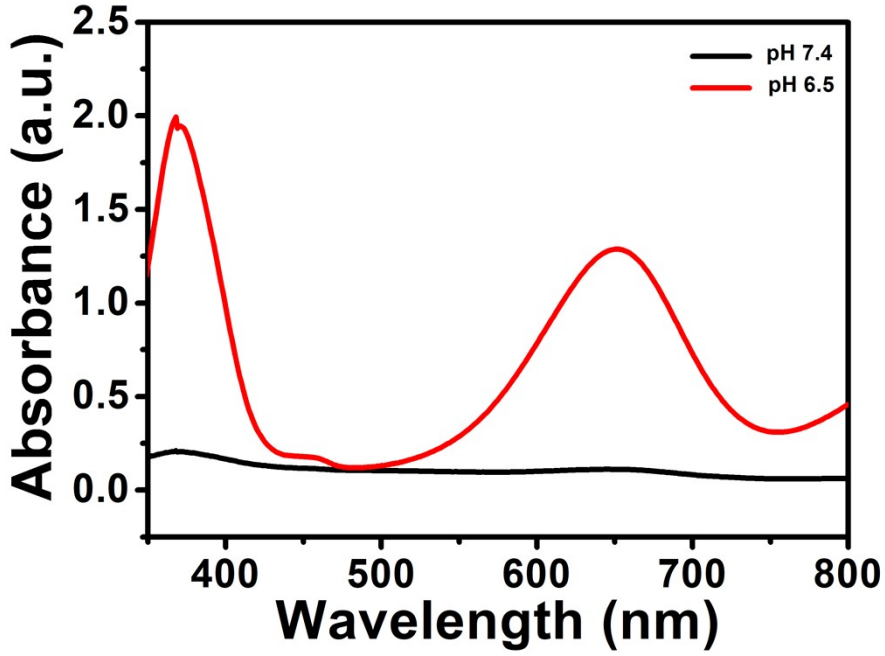


Fig. S9. UV-vis absorption spectra of the catalyzed oxidation of TMB (oxTMB) as catalyzed by DMSN-Au-Fe_3O_4 in different reaction buffers (pH 6.5, pH 7.4).

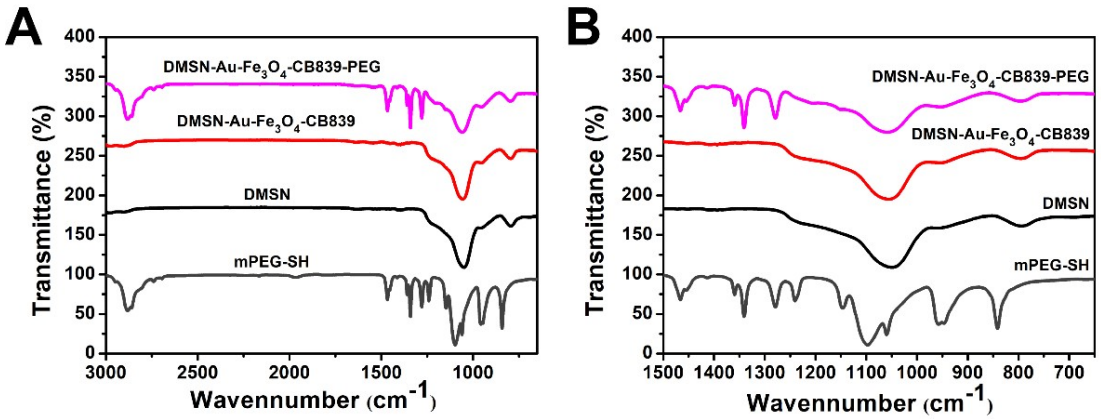


Fig. S10. (A) FTIR spectra of mPEG-SH, DMSN, DMSN-Au-Fe_3O_4-CB839 and DMSN-Au-Fe_3O_4--CB839-PEG samples. (B) Enlarged region of the framed zone in panel A.

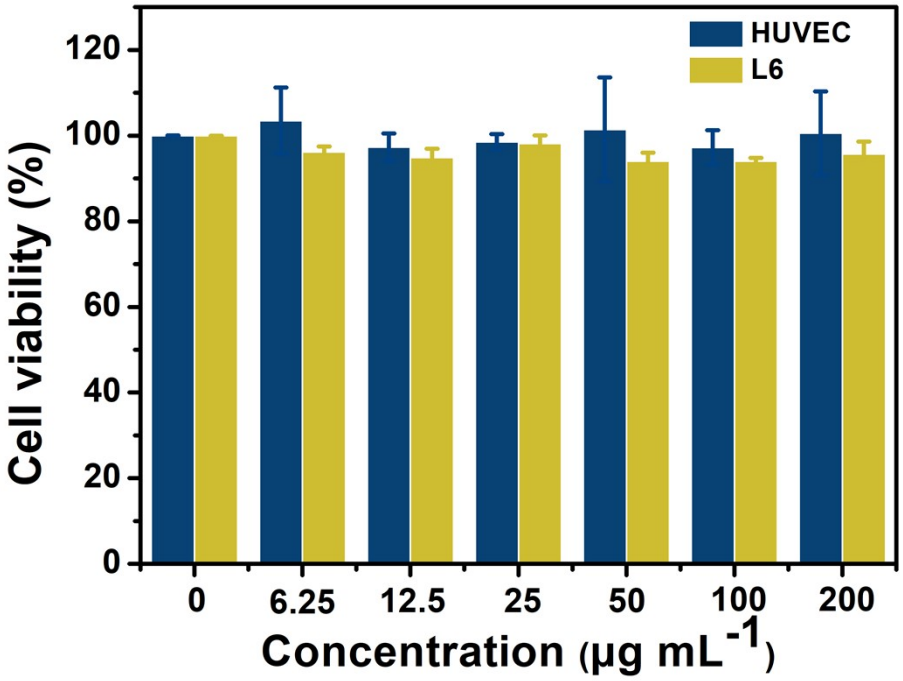


Fig. S11. HUVEC cells and L6 cells treated with various concentrations of DMSN-Au-Fe_3O_4-CB839 for 24 h.

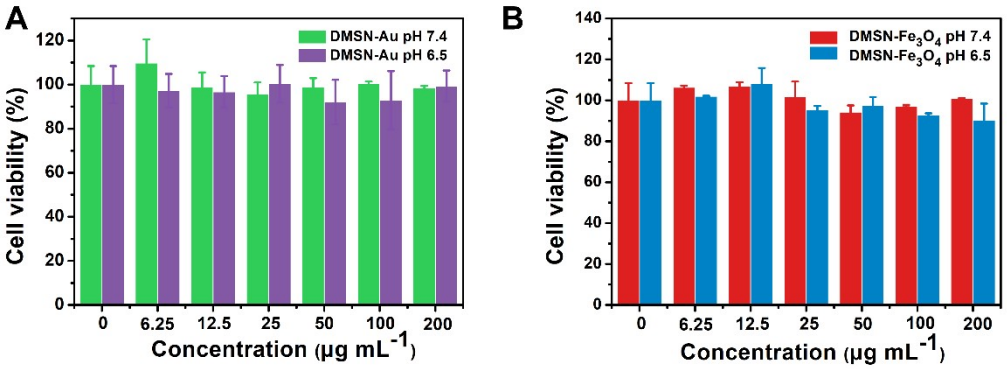


Fig. S12. Relative viabilities of 4T1 cells after being incubated with (A) DMSN-Au NPs and (B) DMSN-Fe_3O_4 NPs at varied concentrations (0, 6.25, 12.5, 25, 50, 100, and 200 μg·mL^{-1}) for 24 h at pH 7.4 and 6.5.

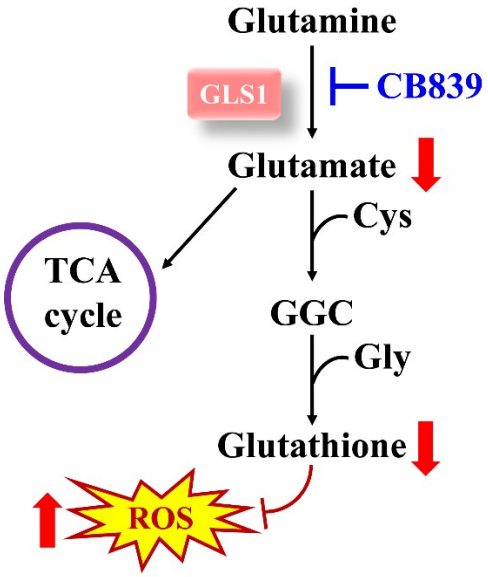
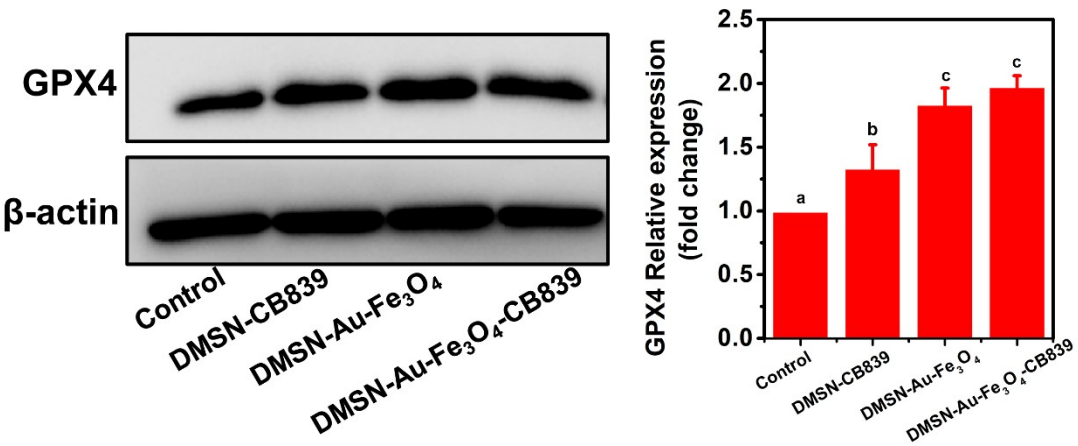


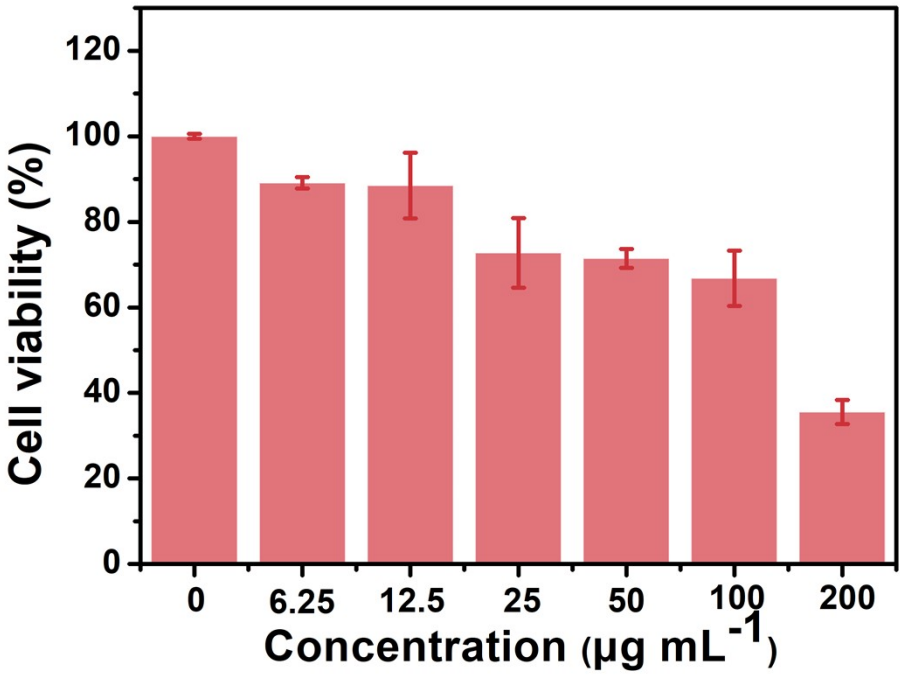
Fig. S13. The synthesis pathway of glutathione.



80

81 Fig. S14. Immunoblot analysis for the expressions of redox indicator proteins GPX4 in

82 4T1 cells. β-actin was used as a loading control.



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84 Fig. S15. A549 cells treated with different concentrations of DMSN-Au-Fe_3O_4-CB839

85 for 24 h.

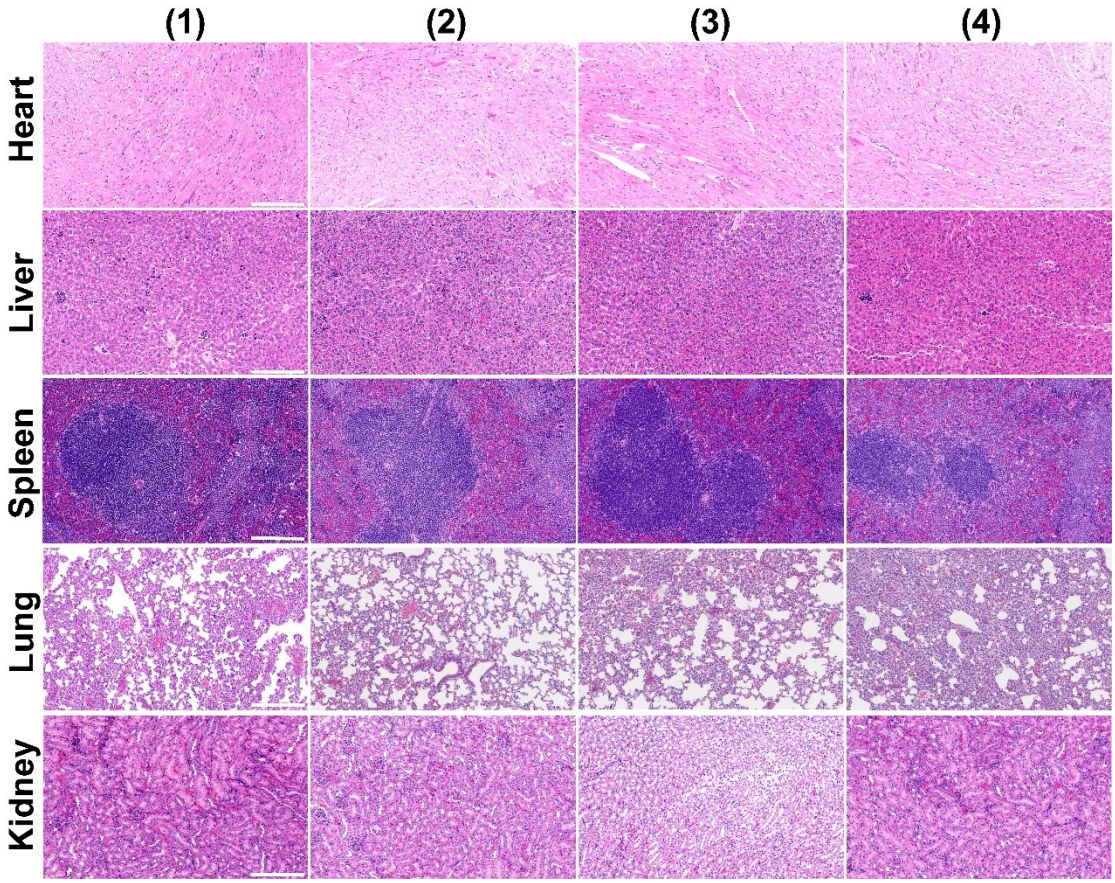

Fig. S16. H&E-stained images of normal tissue (heart, liver, spleen, lung and kidney) of 4T1 tumor-bearing mice treated with different formulations. Scale bars are 200 μm. Groups (1), (2), (3), and (4) represent PBS, DMSN-CB839 (20 $mg \cdot kg^{-1}$), DMSN-Au-Fe_3O_4 (20 $mg \cdot kg^{-1}$), and DMSN-Au-Fe_3O_4-CB839 (20 $mg \cdot kg^{-1}$), respectively.