Supporting Information

Boost therapy of glutamine-addiction glioblastoma by combining glutamine metabolism therapy with photo-enhanced chemodynamic therapy

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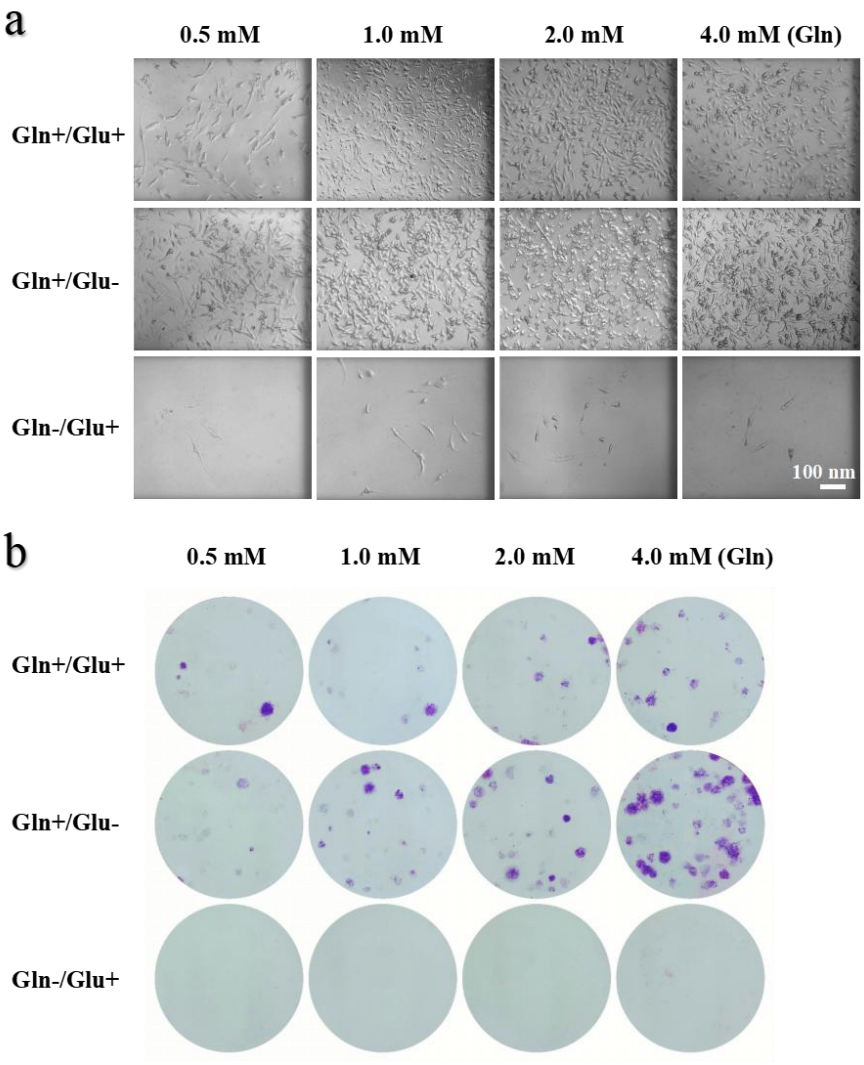

Figure S1. The effect of different glutamine concentrations on the proliferation of U87 MG cells. a) Bright field images of cells cultured within 14 days under different conditions to show the cell proliferation process. b) Corresponding clone formation experiments within 14 days.

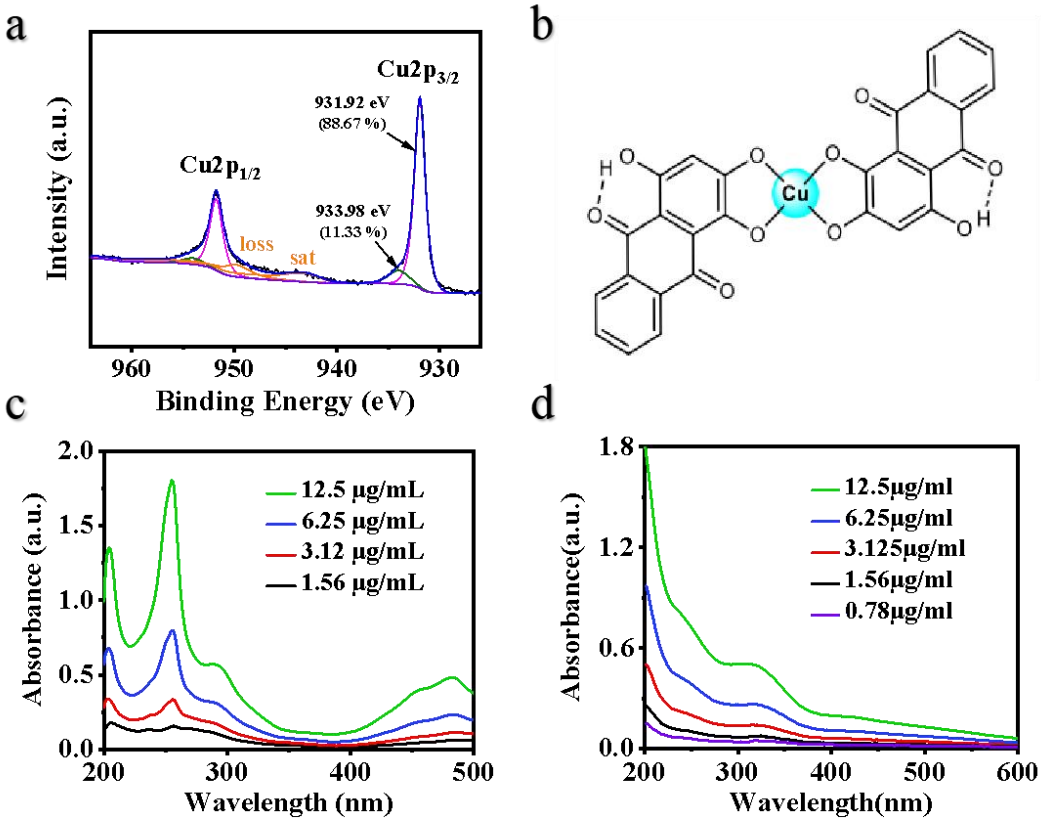

Figure S2. a) High-resolution XPS spectra of Cu2p orbital. b) The possible coordination between copper ions and Purpurin. c) UV-vis absorption of Purpurin with different concentrations. d) UV-vis absorption of CS-P NPs with different concentrations.

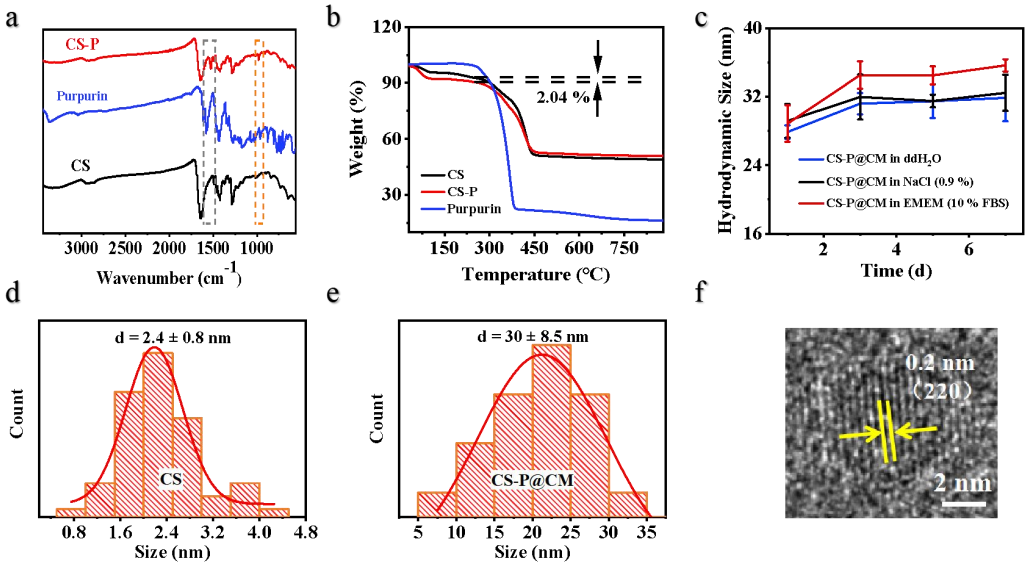

Figure S3. a) FTIR spectra of CS NPs, Purpurin, and CS-P NPs. b) Thermogravimetric analysis of CS NPs, Purpurin, and CS-P NPs. c) The suspension stability of CS-P@CM NPs in EMEM media (10 % FBS), 0.9 % NaCl, and deionized water. Size distributions of d) CS NPs and e) CS-P@CM NPs counted from their TEM images. f) High-resolution TEM image of ultrasmall CS NPs.

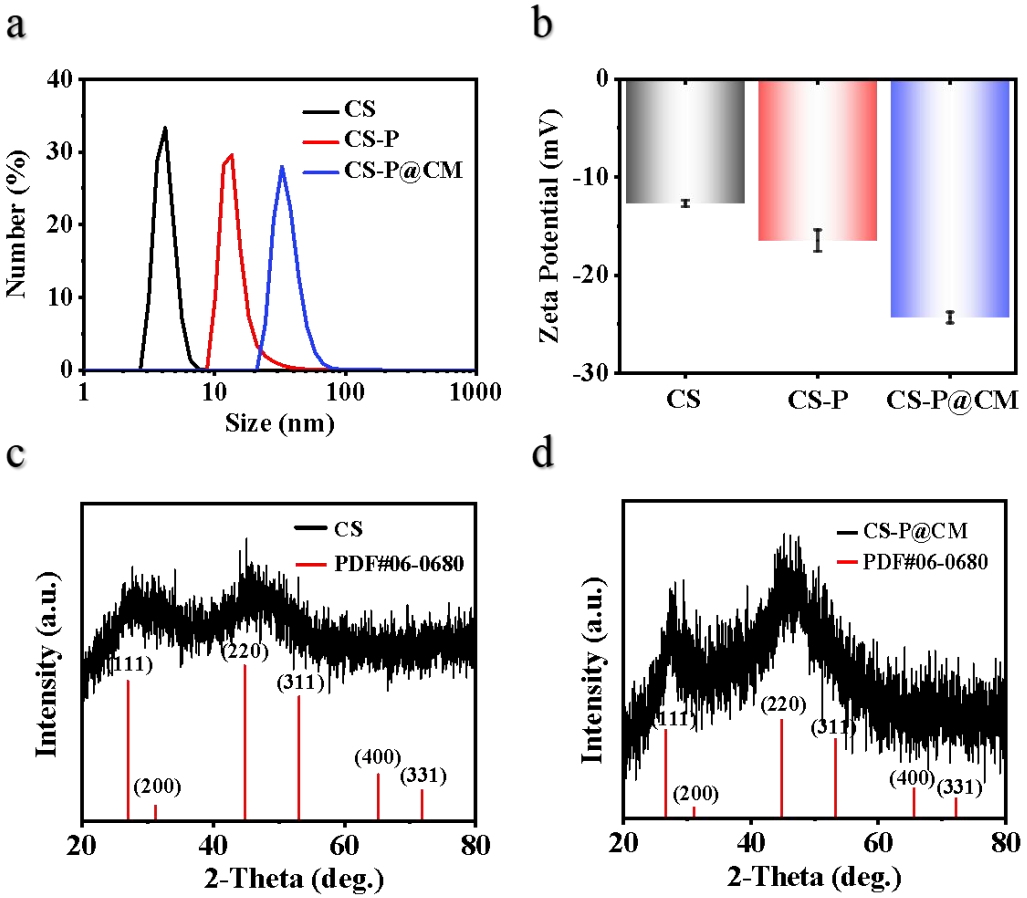

Figure S4. a) Hydrodynamic sizes and b) zeta potentials of CS NPs, CS-P NPs, and CS-P@CM NPs. The XRD patterns of c) CS NPs and d) CS-P@CM NPs.

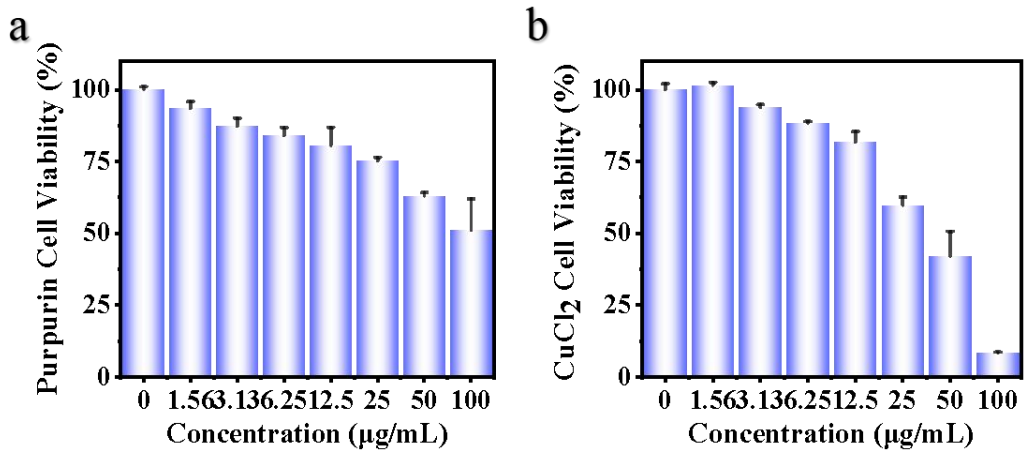

Figure S5. Cytotoxicity of a) Purpurin and b) $CuCl_2$ with different concentrations toward U87 MG cells.

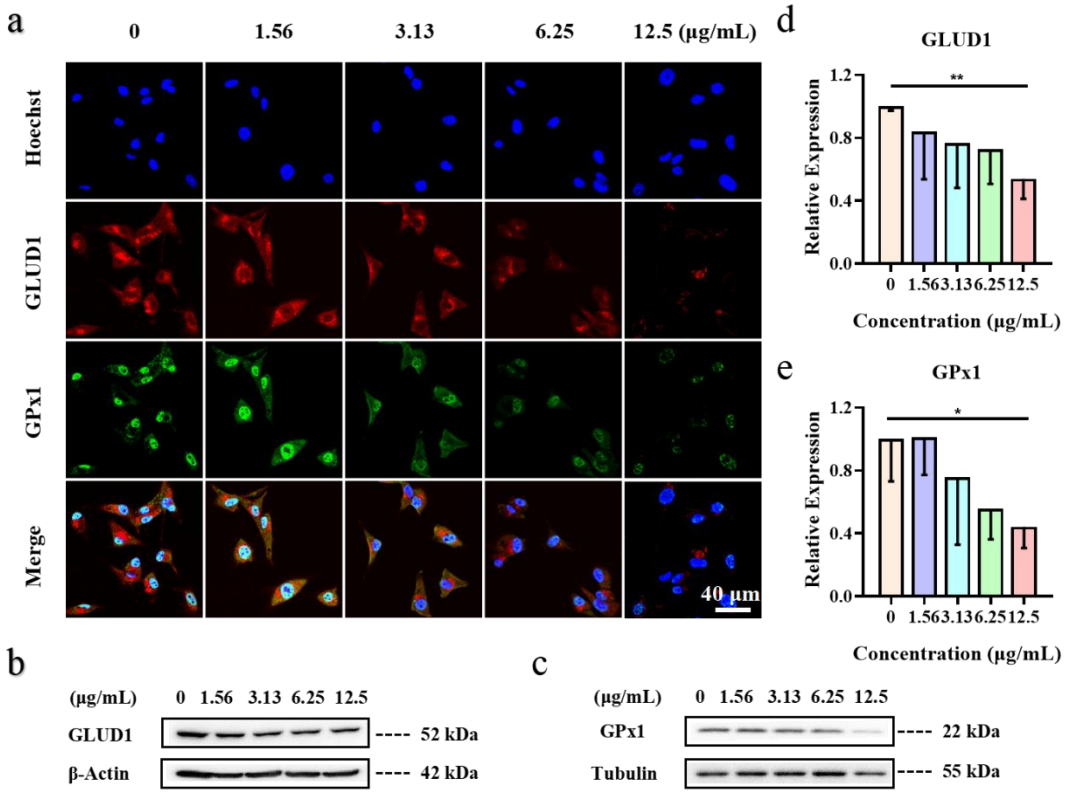

Figure S6. Effects of different concentrations of CS-P@CM NPs on the cellular proteins. a) CLSM images of U87 MG cells cultured with different concentrations of CS-P@CM NPs for 24 h, to show the expressions of GLUD1 (red fluorescence) and GPx1 (green fluorescence). The nuclei were stained blue with Hoechst 33342. The expressions of b) GLUD1 and c) GPx1 proteins after U87 MG cells were cultured with different concentrations of CS-P@CM NPs for 24 h. Quantified expressions of d) GLUD1 and e) GPx1 proteins.

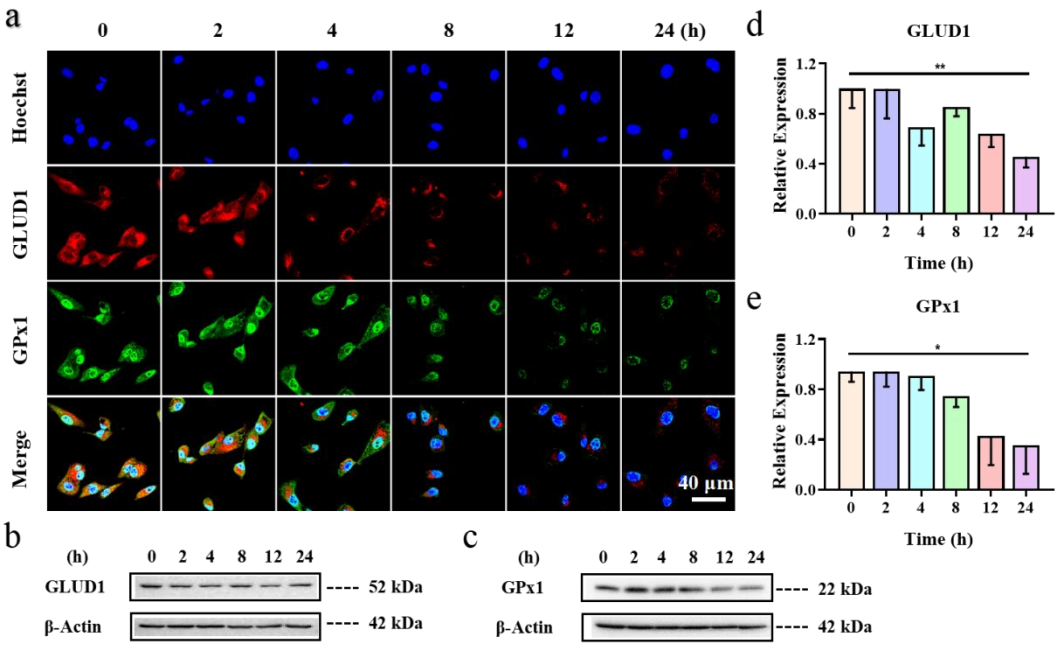

Figure S7. Culture time effects of 12.5 μg/mL CS-P@CM NPs on the cellular proteins. a) CLSM images of U87 MG cells cultured with 12.5 μg/mL CS-P@CM NPs for different time, to show the expressions of GLUD1 (red fluorescence) and GPx1 (green fluorescence). The nuclei were stained blue with Hoechst 33342. The expressions of b) GLUD1 and c) GPx1 proteins after U87 MG cells were cultured with 12.5 μg/mL CS-P@CM NPs for different time. Quantified expressions of d) GLUD1 and e) GPx1 proteins.

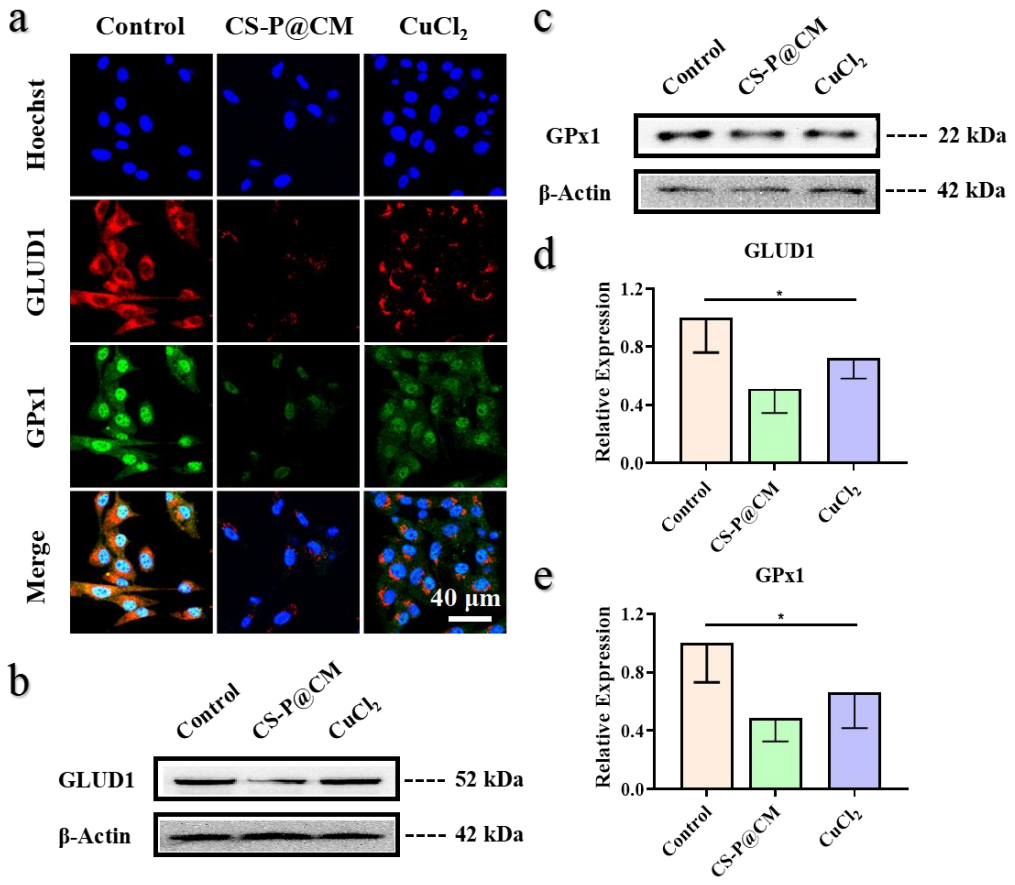

Figure S8. a) CLSM images of U87 MG cells cultured with 12.5 μg/mL CS-P@CM NPs and 12.5 μg/mL $CuCl_2$, respectively, for 24 h, to show the expressions of GLUD1 (red fluorescence) and GPx1 (green fluorescence). The nuclei were stained blue with Hoechst 33342. The expressions of b) GLUD1 and c) GPx1 proteins after U87 MG cells were cultured with CS-P@CM NPs and $CuCl_2$, respectively, for 24 h. Quantified expressions of d) GLUD1 and e) GPx1 proteins.

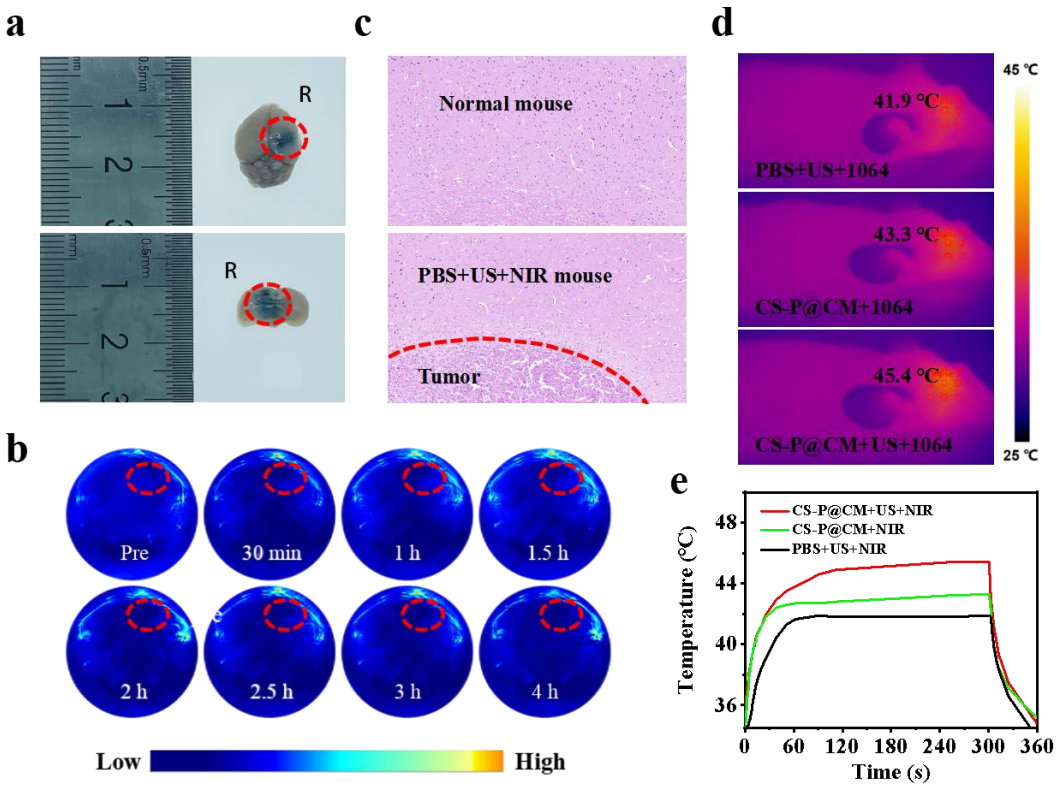

Figure S9. a) Evans blue staining of mouse brains after the mice were treated with focused ultrasound (R: right). b) PA images of the mouse brain before and after injection of CS-P NPs under focused ultrasound at different time points. c) H&E staining of brain slices from healthy mice and the mice treated with PBS + US + NIR (1064 nm, 1 W/cm^2, irradiation time: 5 min). d-e) Thermal images and photothermal heating curves of mice from the PBS + US + NIR, CS-P@CM NPs + NIR, and CS-P@CM NPs + US + NIR groups (CS-P@CM NPs: 500 μg/mL, 200 μL), (1064 nm, 1 W/cm^2, irradiation time: 5 min).

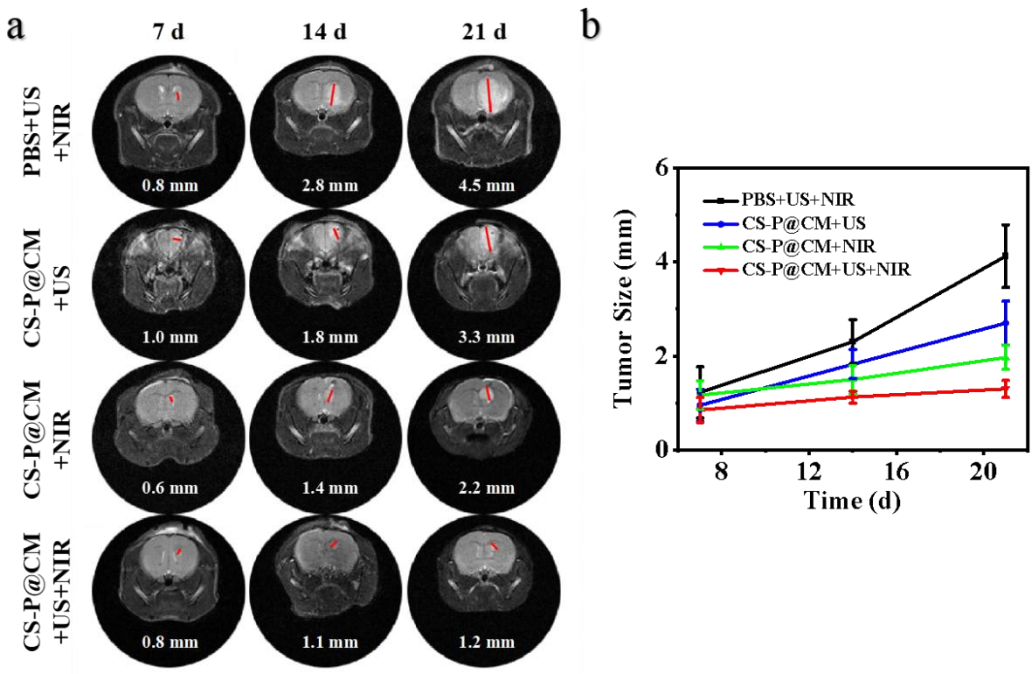

Figure S10. a-b) MRI images and the tumor sizes from different groups of mice before and after treatment.

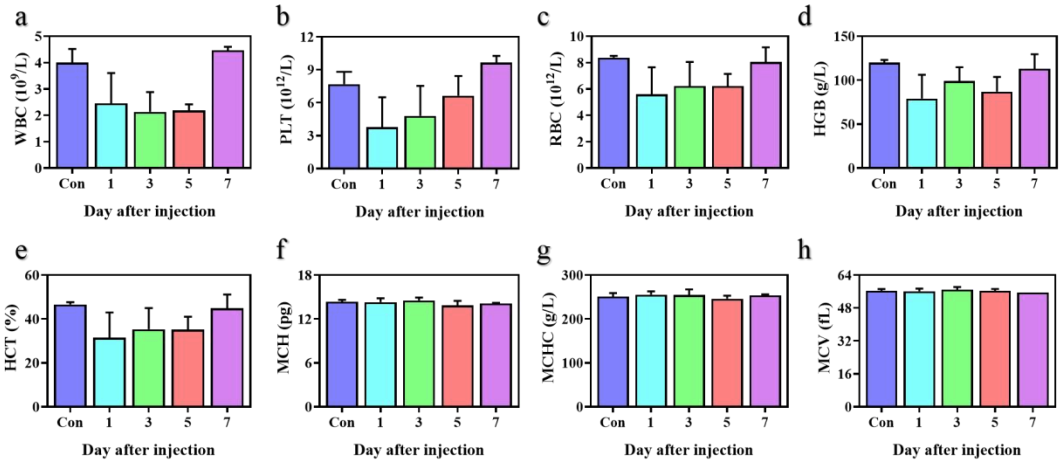

Figure S11. Blood routine examinations of the mice injected with CS-P@CM NPs (500 μg/mL, 200 μL) on day 0, 1, 3, 5, and 7. Abbreviations: a）white blood cell count, WBC; b) platelet count, PLT; c) red blood cell count, RBC; d) hemoglobin, HGB; e) hematocrit, HCT; f) mean corpuscular hemoglobin, MCH; g) mean corpuscular hemoglobin concentration, MCHC; h) mean corpuscular volume, MCV.