Supporting Information for

## **Biomineralization-Inspired Synthesis of Copper Sulfide-Ferritin Nanocages as Cancer Theranostics**

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## Translator

## Translate DNA and RNA sequences to protein sequences.



**Figure S2.** (a) Open reading frame of the rat ferritin heavy chain for CuS-Fn NCs synthesis. (b) ESI-MS analysis of Ferritin.



Figure S3. Comparison of ferritin and CuS-Fn NCs samples with or without uranyl acetate staining.



**Figure S4.** (a) HAADF-STEM image of CuS-Fn NCs. (b) High resolution line-scan EDS analysis of CuS-Fn-NCs. (c) Area-scan EDS analysis of CuS-Fn-NCs.



**Figure S5.** (a) Photothermal effect of the irradiation of the aqueous dispersion of CuS-Fn NCs (80  $\mu$ g/mL) with the NIR laser (808 nm, 0.2 W/cm<sup>2</sup>), in which the irradiation lasted for 5 min, and then the laser was turned off. (b) Time constant for heat transfer from the system is determined to be  $\tau_s = 70.55$  s by applying the linear time data from the cooling period (after 300 s) versus negative natural logarithm of driving force temperature, which is obtained from the cooling stage of panel 1.



Figure S6. Photoacoustic images of PBS (Control) and CuS-Fn ( $80 \mu g/mL$ ) solution.



Figure S7. UV-vis absorbance spectrum of CuS nanoparticle.



Figure S8. (1) DLS analysis of CuS nanoparticle. (2) TEM image of CuS nanoparticle .



**Figure S9.** (a) Cell toxicity and photothermal efficiency of CuS. (b) Photothermal efficiency comparison between CuS nanoparticle and CuS-Fn NCs.



**Figure S10.** Cellular uptake of CuS-Fn-Cy 5.5 on different cell lines: U87MG, A549, PC3, HepG2 cells.



**Figure S11.** Multi-slice confocal image of U87 MG cell after CuS-Fn-Cy 5.5 treatment. (Blue: DAPI, Green: Alexa 488 conjugated phalloidin, Red: CuS-Fn-Cy 5.5)



Figure S12. 2D photoacoustic images of U87 MG tumor of different time point after CuS-Fn NCs injection.



**Figure S13.** a. PA signal of tumor region amplitude after CuS-Fn NCs injection. b. PA amplitude comparison between tumor region and background.



**Figure S14.** TLC plate analyses of  $^{64}$ CuS-Fn NCs after incubation with Na-acetate for 10 min (a) and 24 h (b).



**Figure S15.** TLC plate analyses of <sup>64</sup>Cu-acetate.



Figure S16. Ex vivo PET image of major organ and tumor 24 h after CuS-Fn NCs injection.



Figure S17. H&E staining of tumors.



Figure S18. H&E staining of major organs.