

## Supporting Information

### **Modulation of Intratumoral *Fusobacterium nucleatum* to Enhance Sonodynamic Therapy for Colorectal Cancer with Reduced Phototoxic Skin Injury**

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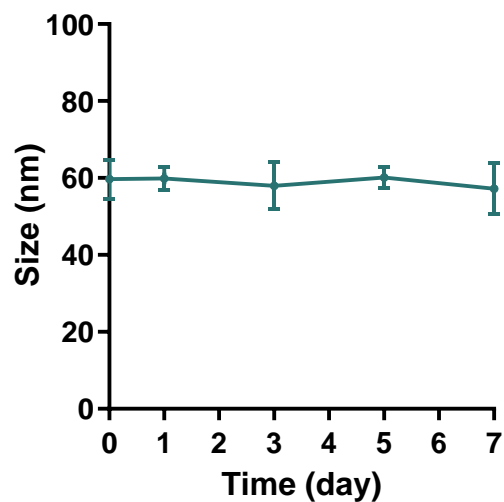
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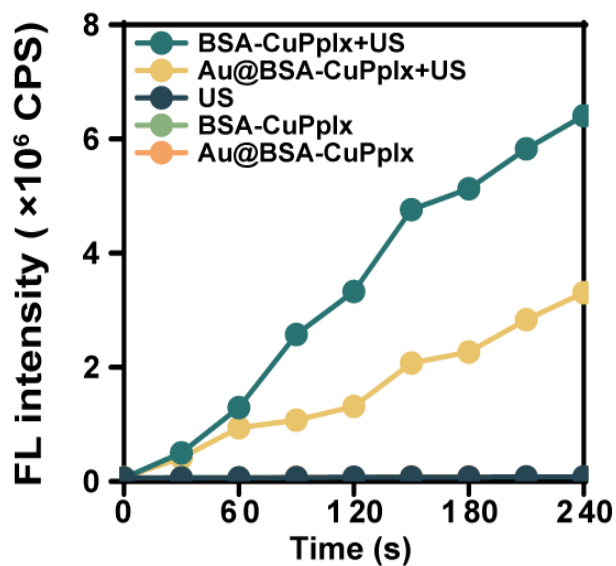
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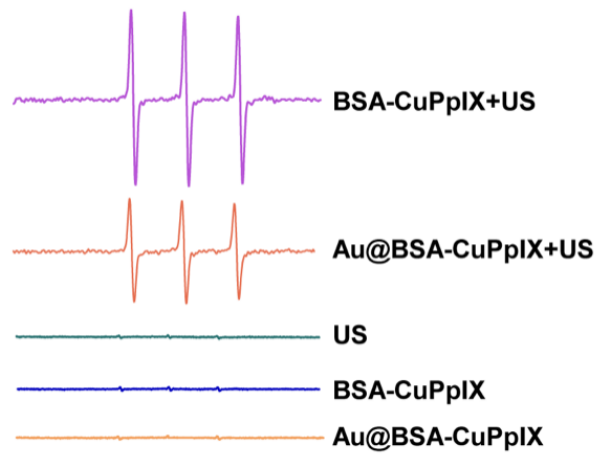
‡ The authors contributed equally to this paper.



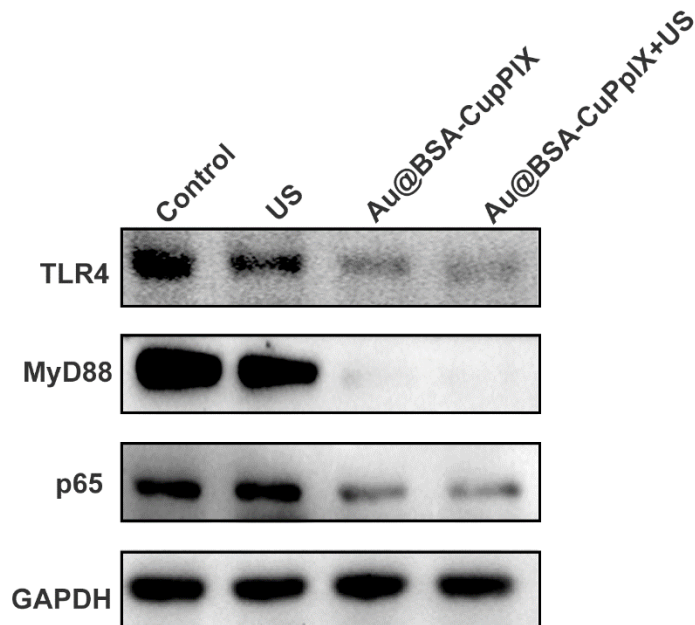
**Figure S1.** The average diameter of Au@BSA-CuPpIX in 7 days.



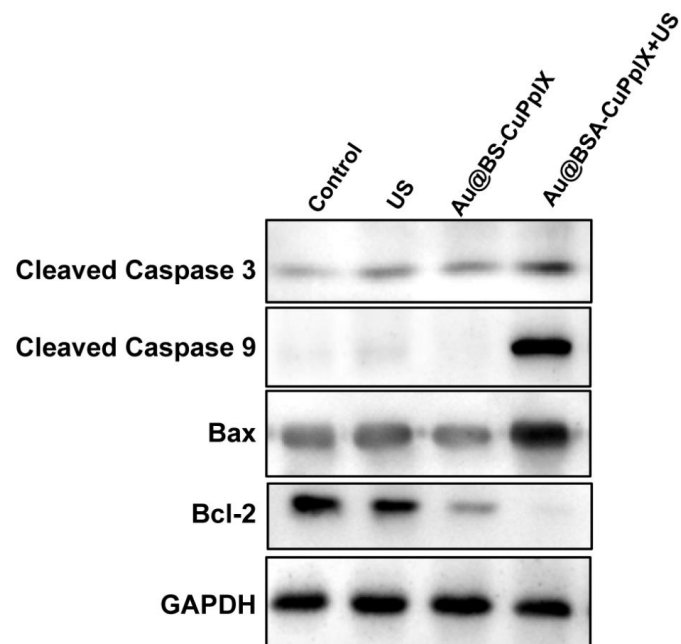
**Figure S2.** Fluorescence intensity of single oxygen sensor green (SOSG) under different conditions with or without US radiation.



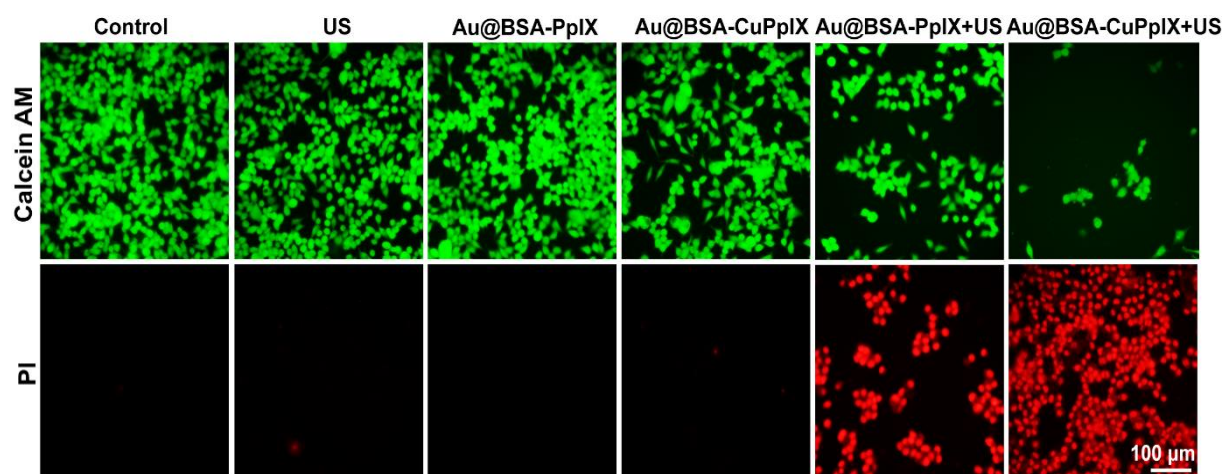
**Figure S3.** ESR spectra of BSA-CuPpIX+US, Au@BSA-CuPpIX+US, US, BSA-CuPpIX, and Au@BSA-CuPpIX groups, TEMP as a trapping agent.



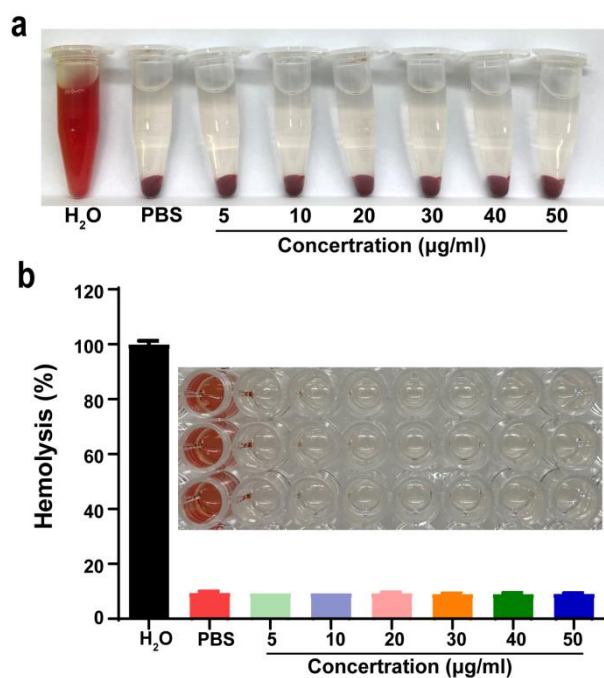
**Figure S4.** Western blot analysis of the expression of TLR4, MyD88, and p65 in various treatments of HCT116 cells. HCT116 cells were co-cultured with *F. nucleatum* for 48 h before treatments.



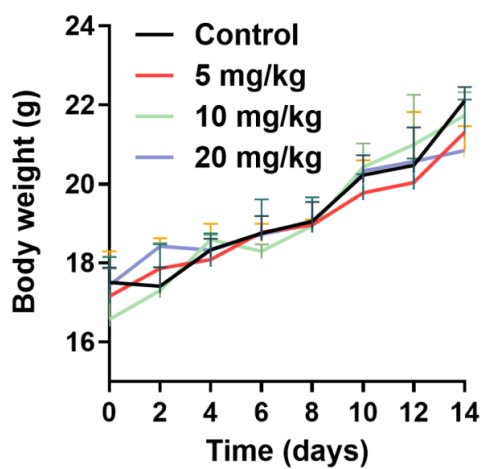
**Figure S5.** Western blot analysis of the expression of the apoptosis-related proteins (Cleaved Caspase 3, Cleaved Caspase 9, Bax, Bcl-2) in various treatments of HCT116 cells protein.



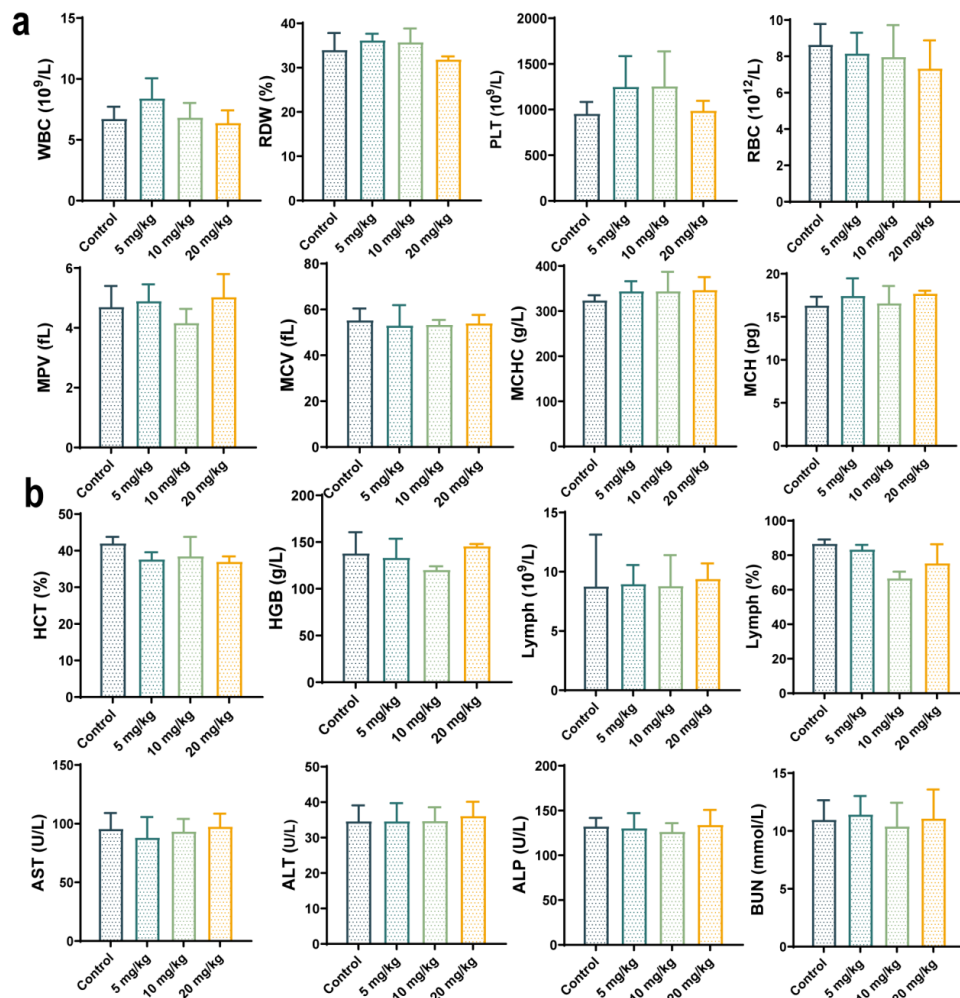
**Figure S6.** Inverted fluorescence microscope images of HCT116 cells stained by Calcein-AM&PI dyes in different treatments (Green fluorescence: calcein AM representing living cells, red fluorescence: PI representing dead cells).



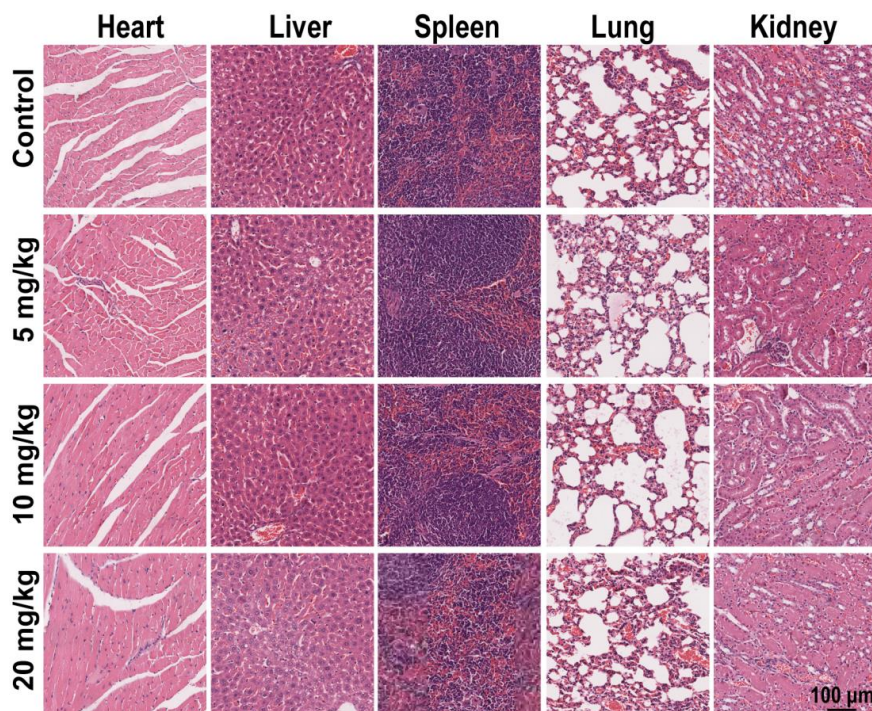
**Figure S7.** a) The hemolysis of blood cells in the different concentrations of Au@BSA-CuPpIX treatments. b) The ratio of hemolysis in the subgroups.



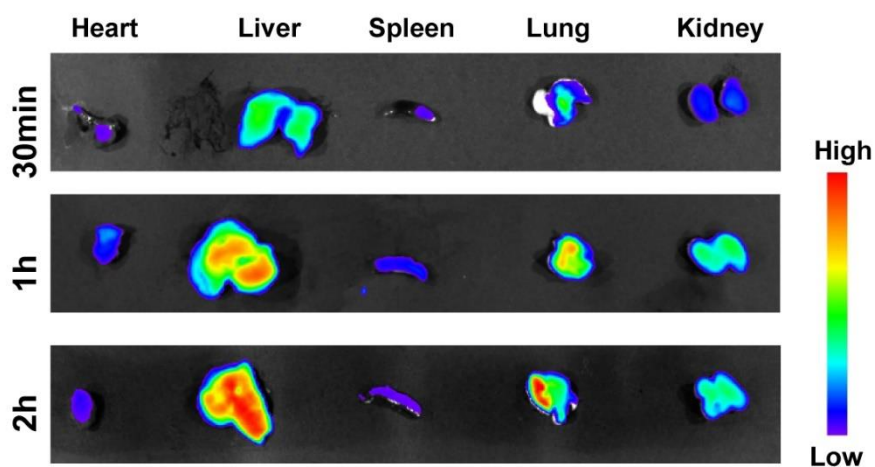
**Figure S8.** Mice's body weight after receiving different concentrations of Au@BSA-CuPpIX ( $5 \text{ mg kg}^{-1}$ ,  $10 \text{ mg kg}^{-1}$ ,  $20 \text{ mg kg}^{-1}$ ) treatments.



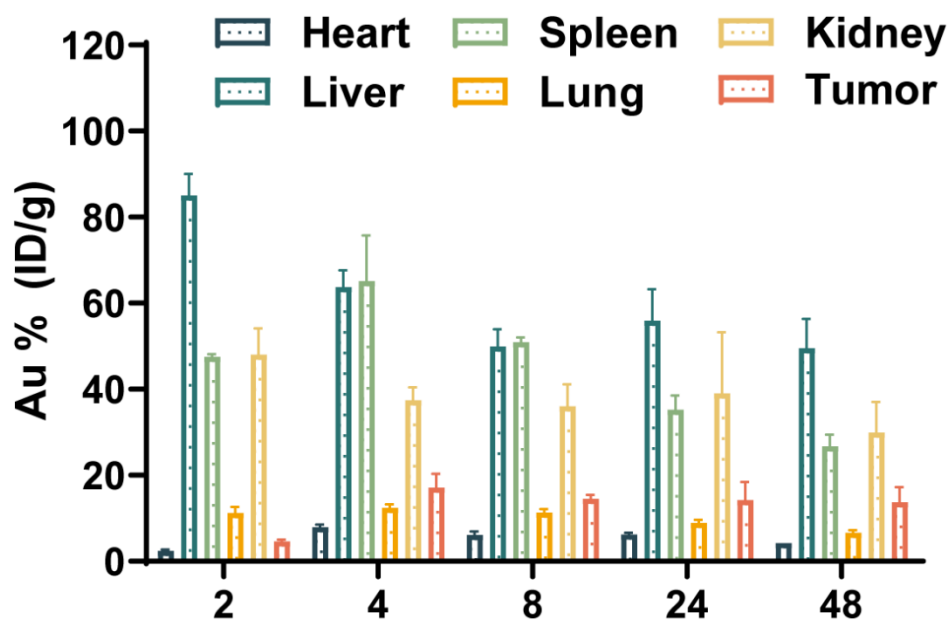
**Figure S9.** a) and b) Hematological index and biochemical blood analysis of mice after intravenous injection with different concentrations of Au@BSA-CuPpIX ( $5 \text{ mg kg}^{-1}$ ,  $10 \text{ mg kg}^{-1}$ ,  $20 \text{ mg kg}^{-1}$ ) treatments.



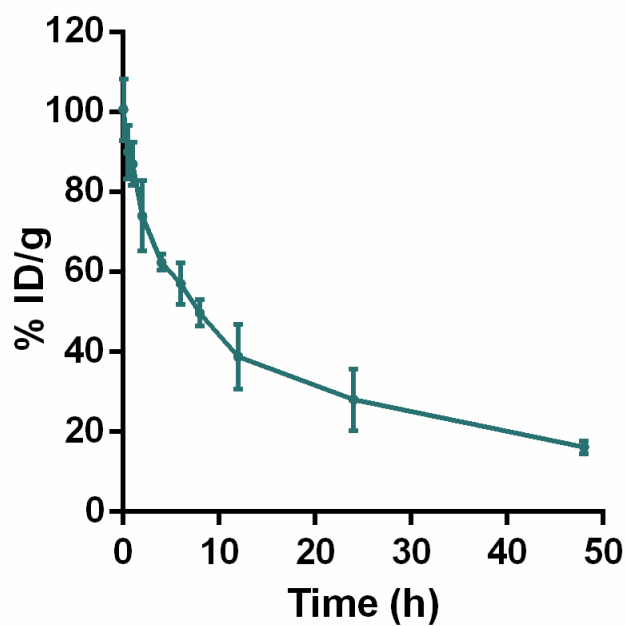
**Figure S10.** H&E staining of right kidney, heart, liver, spleen and lung after receiving different concentrations of Au@BSA-CuPpIX ( $5 \text{ mg kg}^{-1}$ ,  $10 \text{ mg kg}^{-1}$ ,  $20 \text{ mg kg}^{-1}$ ) treatments.



**Figure S11.** The fluorescence signal of cy5.5-labeled Au@BSA-CuPpIX in organs of mice after intravenous injection at 30 min, 1 h and 2 h.

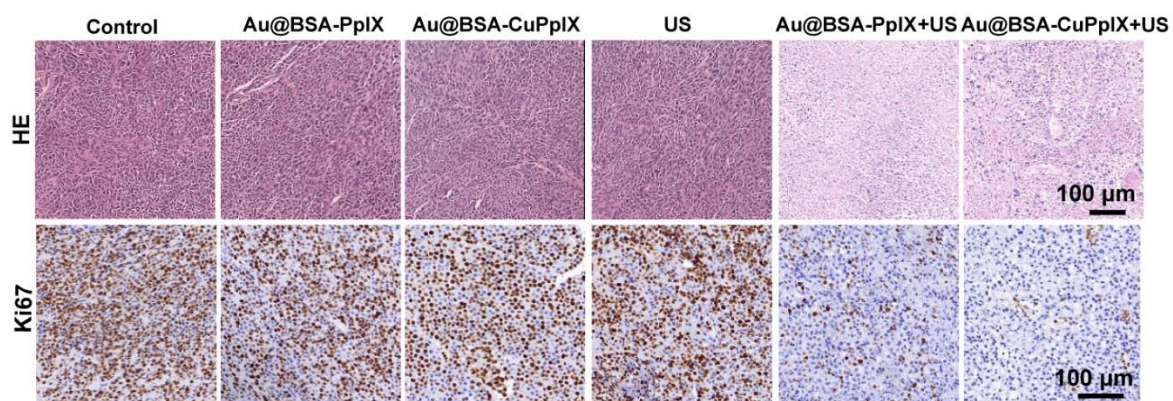


**Figure S12.** Analysis of Au NPs biodistribution in the Heart, kidney, lung, spleen, liver and tumor at 48h. The data are presented as the mean  $\pm$  SD.

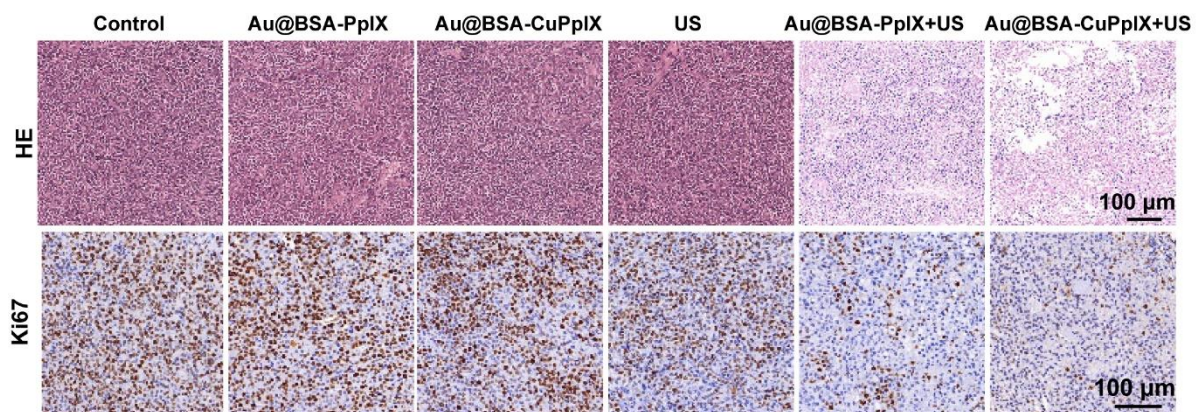


**Figure S13.** Blood-circulation curve in rats injected intravenously with Au@BSA-CuPpIX (Mean  $\pm$  SD, n=3)





**Figure S14.** Representative HE, Ki67 stained sections of HCT116 tumor tissue at the end of the experiments in a subcutaneously implanted tumor model in a nude mouse.



**Figure S15.** HE and Ki67 staining of the tumor after different treatments in the orthotopic CRC model.