

Supporting Information for

Original article

**Biodegradable calcium sulfide-based nanomodulators for
H₂S-Boosted Ca²⁺-involved synergistic cascade cancer
therapy**

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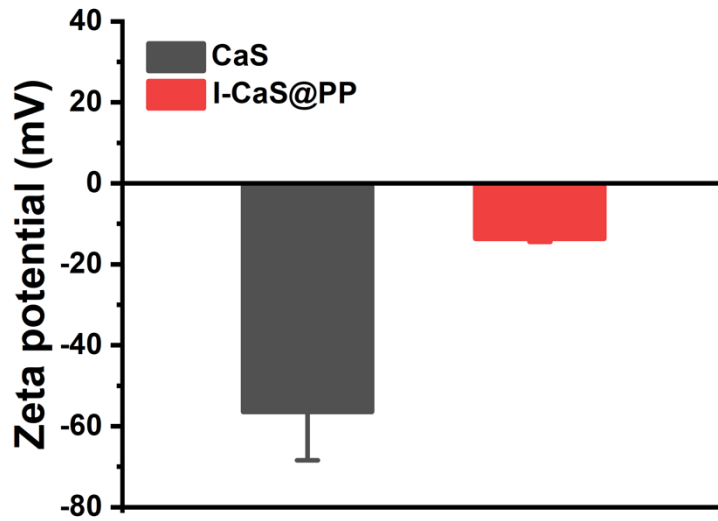


Figure S1 Zeta potentials of CaS and I-CaS@PP. Data are presented as the mean \pm SD (n = 3).

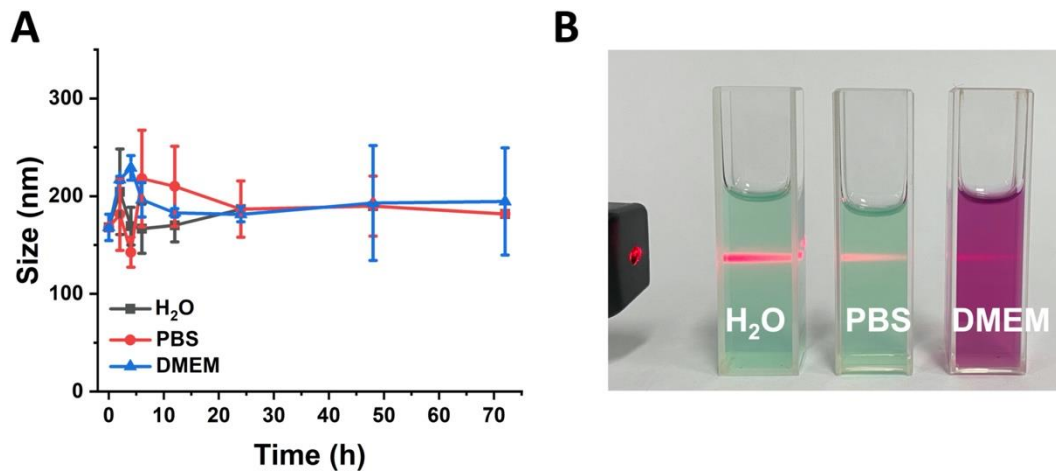


Figure S2 (A) Size changes and (B) digital photographs of I-CaS@PP after incubation in water, PBS and DMEM containing 10% FBS at 37 °C. The data are presented as the mean \pm SD (n = 3).

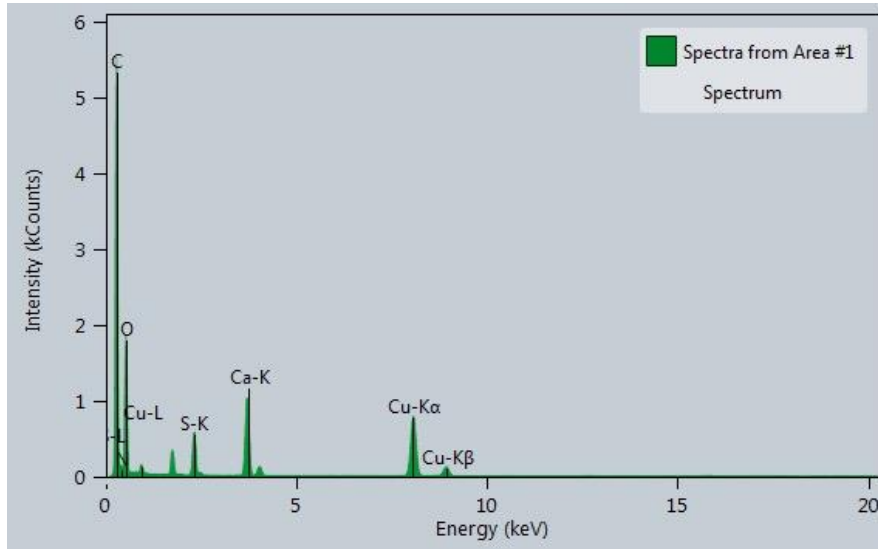


Figure S3 Energy dispersive X-ray spectroscopy (EDX) of I-CaS@PP.

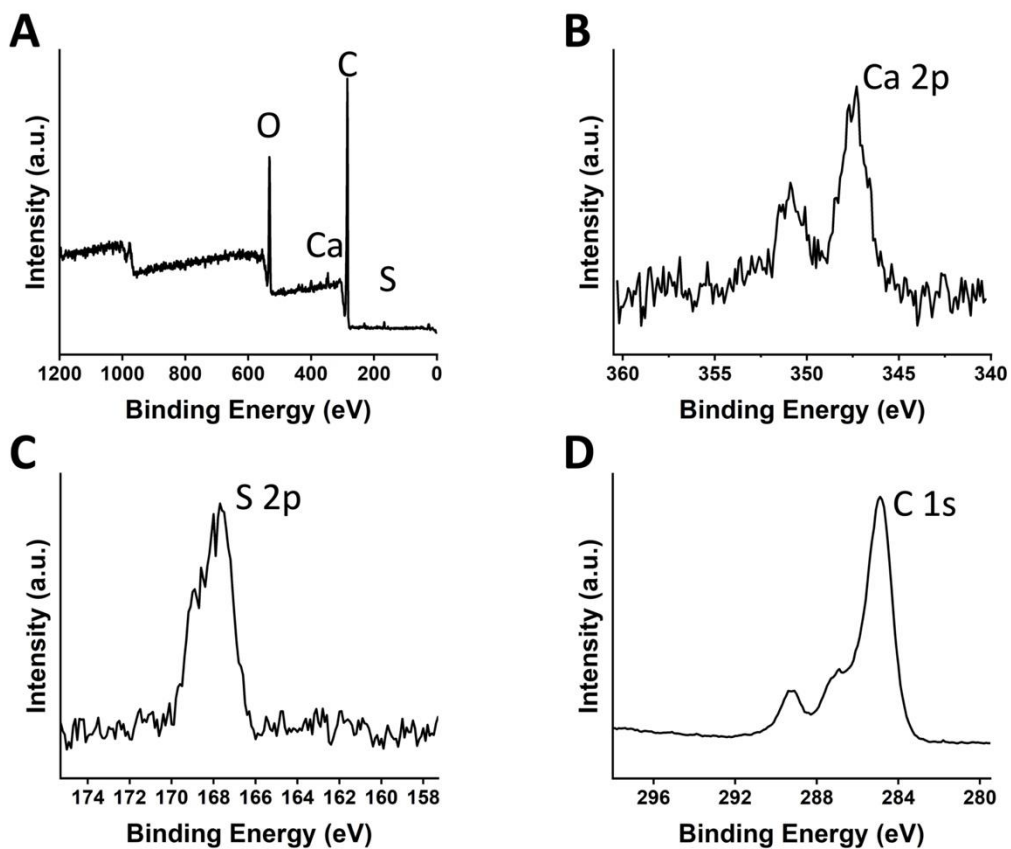


Figure S4 X-ray photoelectron spectrum (XPS) of (A) I-CaS@PP, and (B) Ca 2p, (C) S 2p, (D) C 1s in I-CaS@PP.

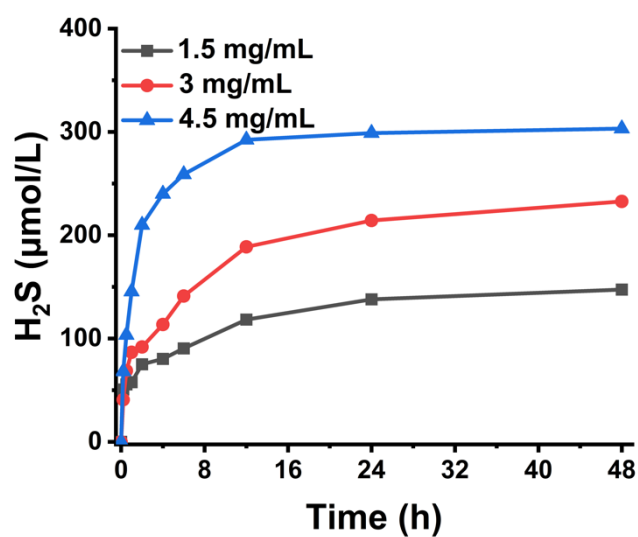


Figure S5 Concentration-dependent H₂S release profile from I-CaS@PP at pH 5.5.

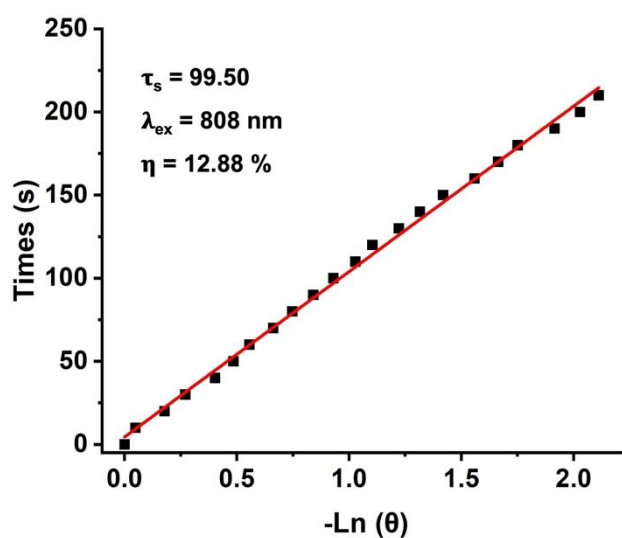


Figure S6 Corresponding linear relationship between time and $-\ln\theta$ from the cooling period under 808 nm laser irradiation (1.2 W cm^{-2}).

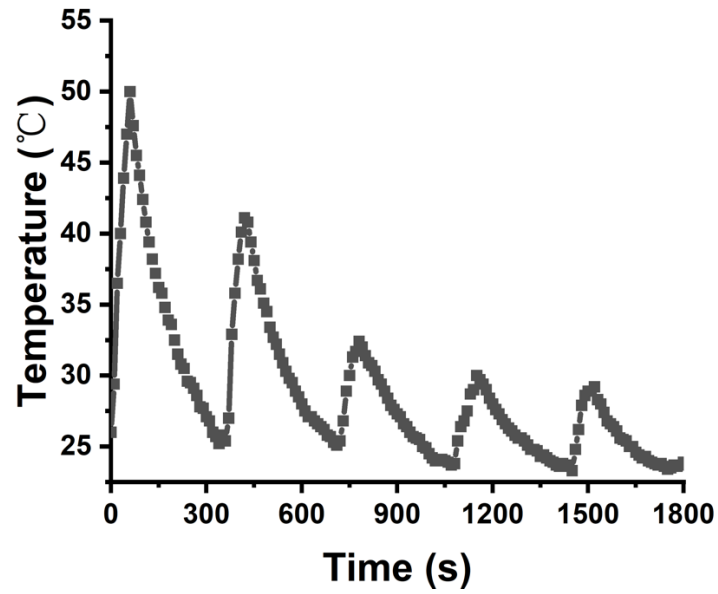


Figure S7 Photothermal conversion stability of free ICG aqueous solution for five laser on/off cycles with an 808 nm laser irradiation (1.2 W cm^{-2}).

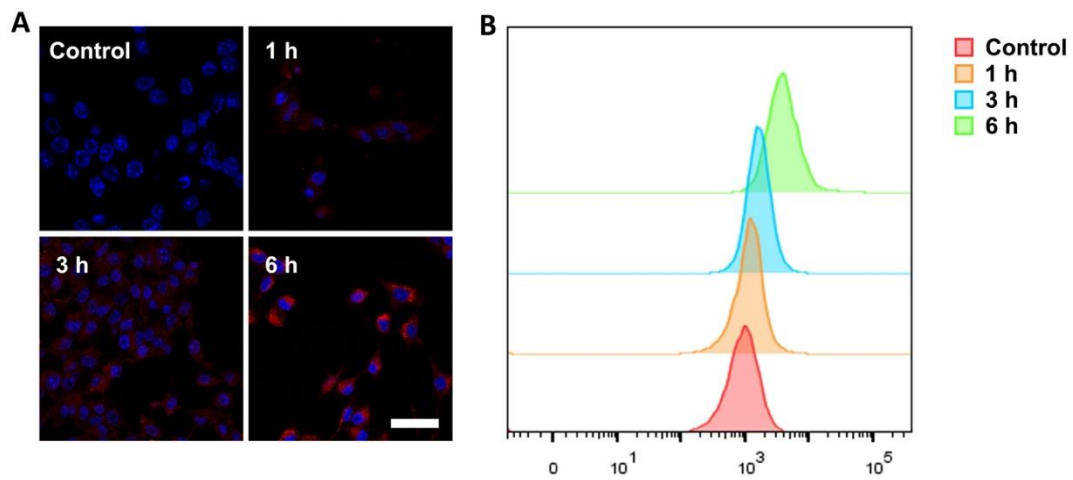


Figure S8 CLSM images and flow cytometry analysis of cellular uptake in 4T1 cells at different time points. Scale bar = $50 \mu\text{m}$.

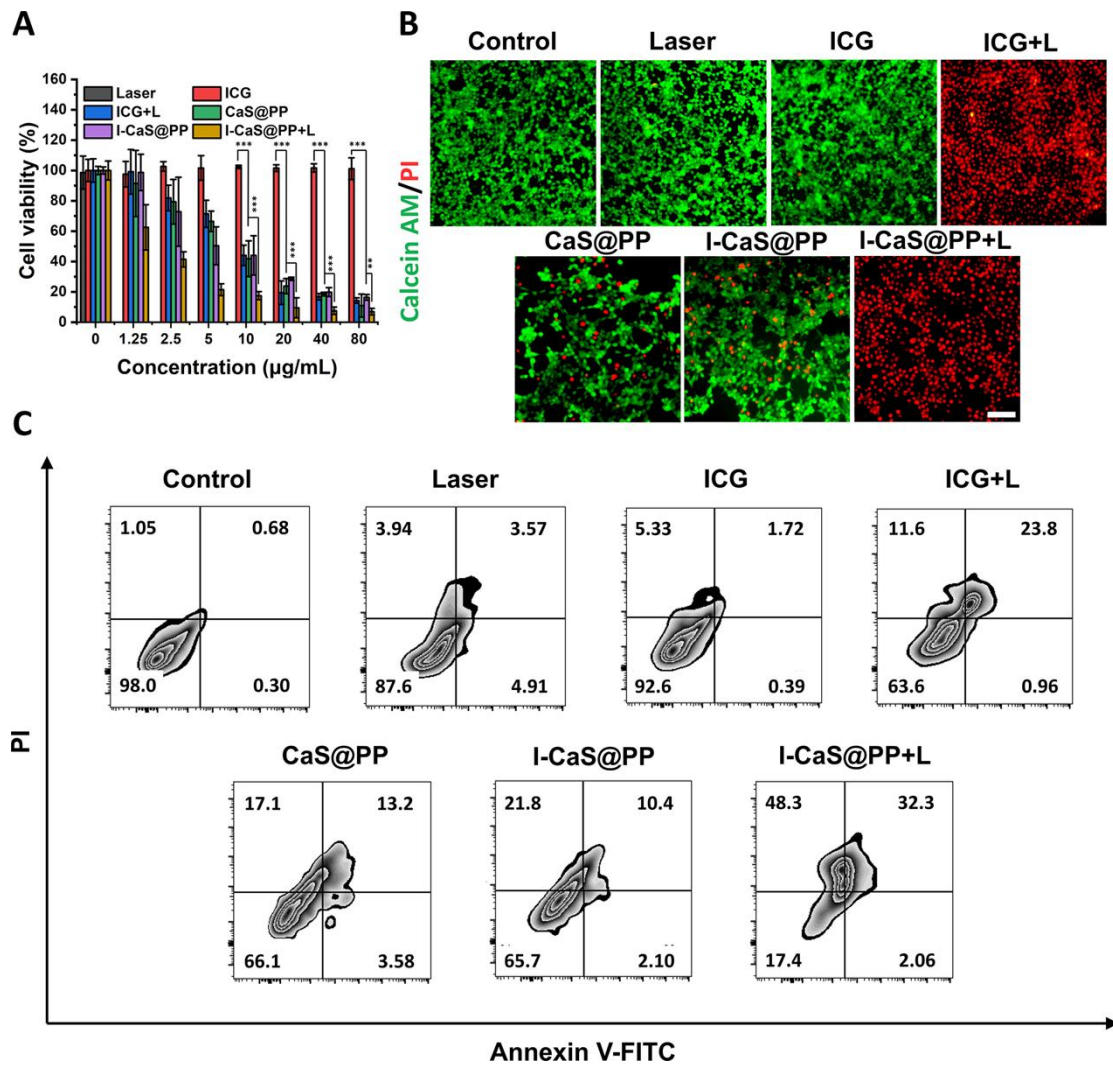


Figure S9 (A) Cell viability of 4T1 cells after treated with different concentrations of ICG, CaS@PP and I-CaS@PP with or without laser irradiation at 24 h incubation. (B) Live/dead dual staining of 4T1 cells after different treatments for 24 h. Scale bar = 200 μm . (C) *In vitro* apoptosis-inducing effects on 4T1 cells after different treatments determined by flow cytometry analysis. Data are presented as mean \pm SD ($n = 3$). ** $P < 0.01$, *** $P < 0.001$.

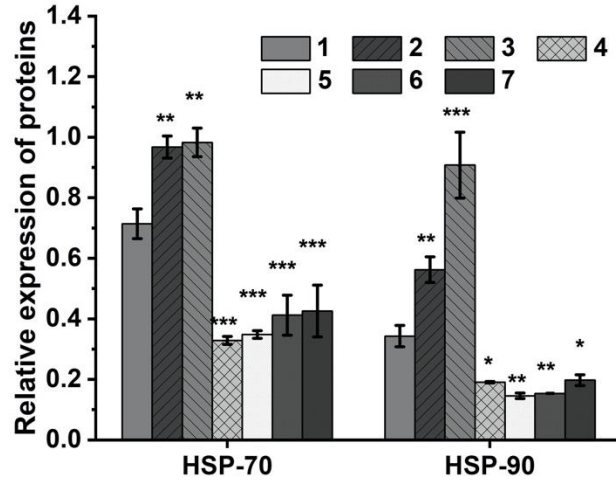


Figure S10 Quantification of protein expression of HSP-70 and HSP-90. 1: Control; 2: Control + 40 °C; 3: CaCl₂ + 40 °C; 4: CaS@PP; 5: I-CaS@PP; 6: I-CaS@PP + L; 7: I-CaS@PP + L + EGTA. Data are presented as mean ± SD (n = 3). **P* < 0.05, ***P* < 0.01 and ****P* < 0.001 vs group 1.

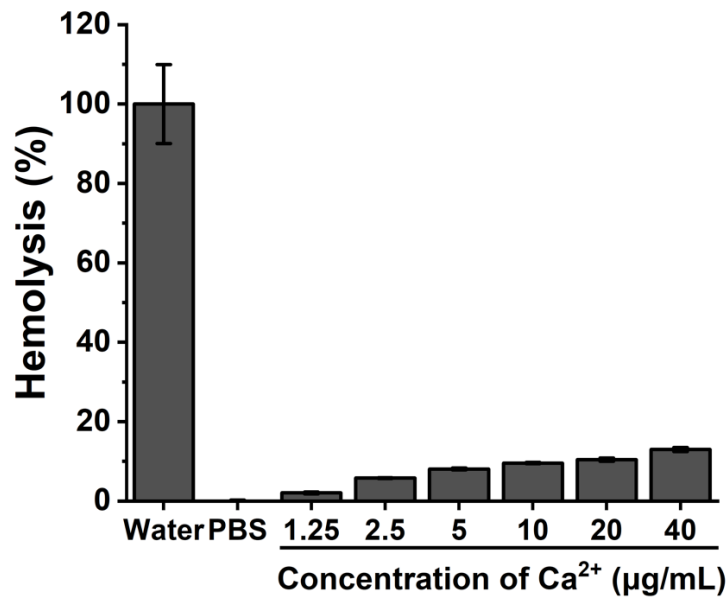


Figure S11 Hemolysis quantification of red blood cells treated with water, PBS and I-CaS@PP dispersed in PBS at different Ca²⁺ concentrations (1.25, 2.5, 5, 10, 20 and 40 µg/mL). Data are presented as mean ± SD (n = 3).

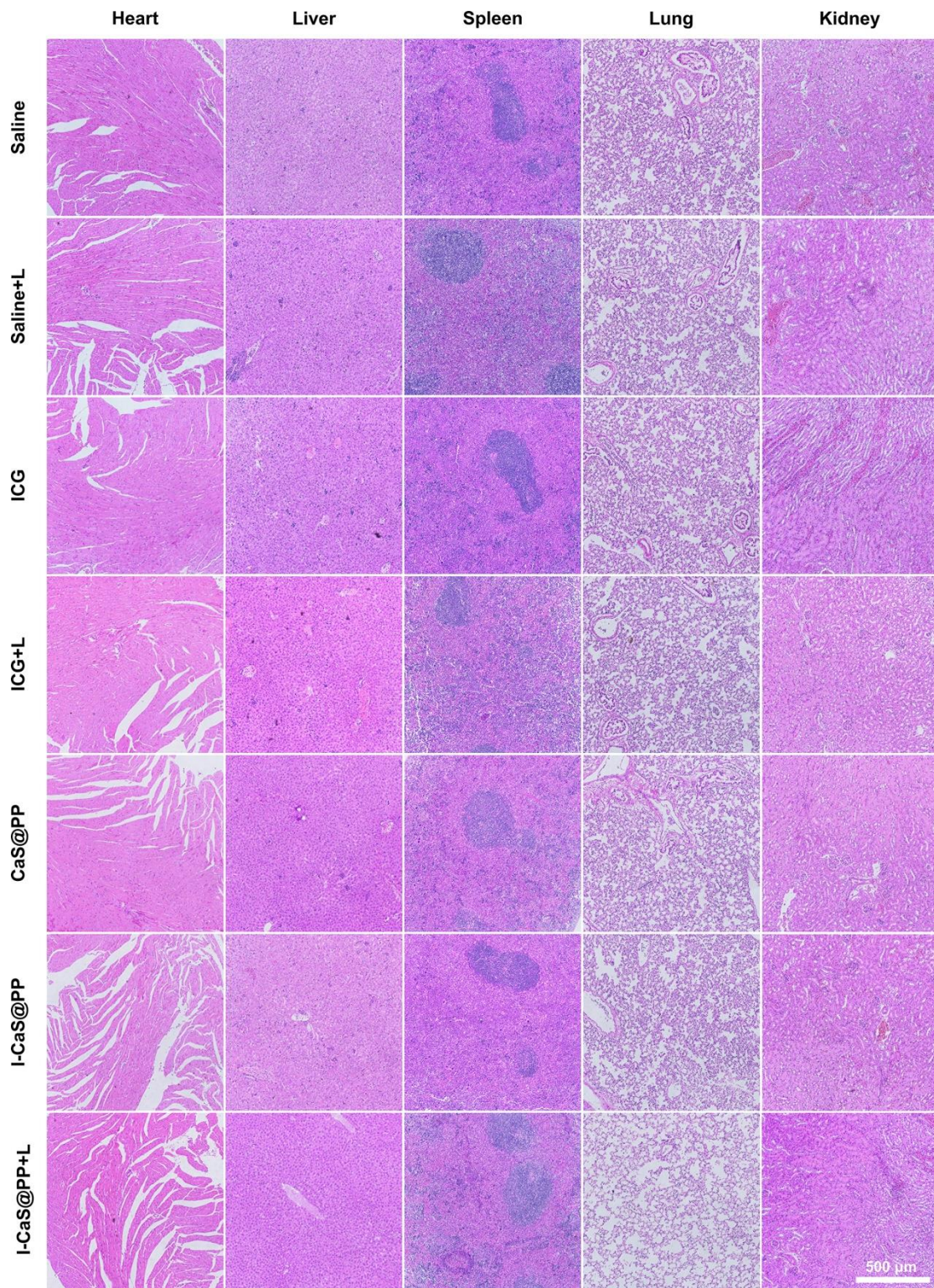


Figure S12 HE stained organ slices from 4T1-bearing mice with different treatments.

References:

1. Zhang MR, Zheng W, Liu Y, Huang P, Gong ZL, Wei JJ, et al. A new class of blue-LED-excitabile NIR-II luminescent nanoprobe based on lanthanide-doped CaS nanoparticles. *Angew Chem Int Ed* 2019; **58**: 9556-9560.