Supporting Information

of

Enzyme-Driven Membrane-Targeted Chimeric Peptide for Enhanced Tumor Photodynamic-Immunotherapy

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†These authors contributed equally to this work.

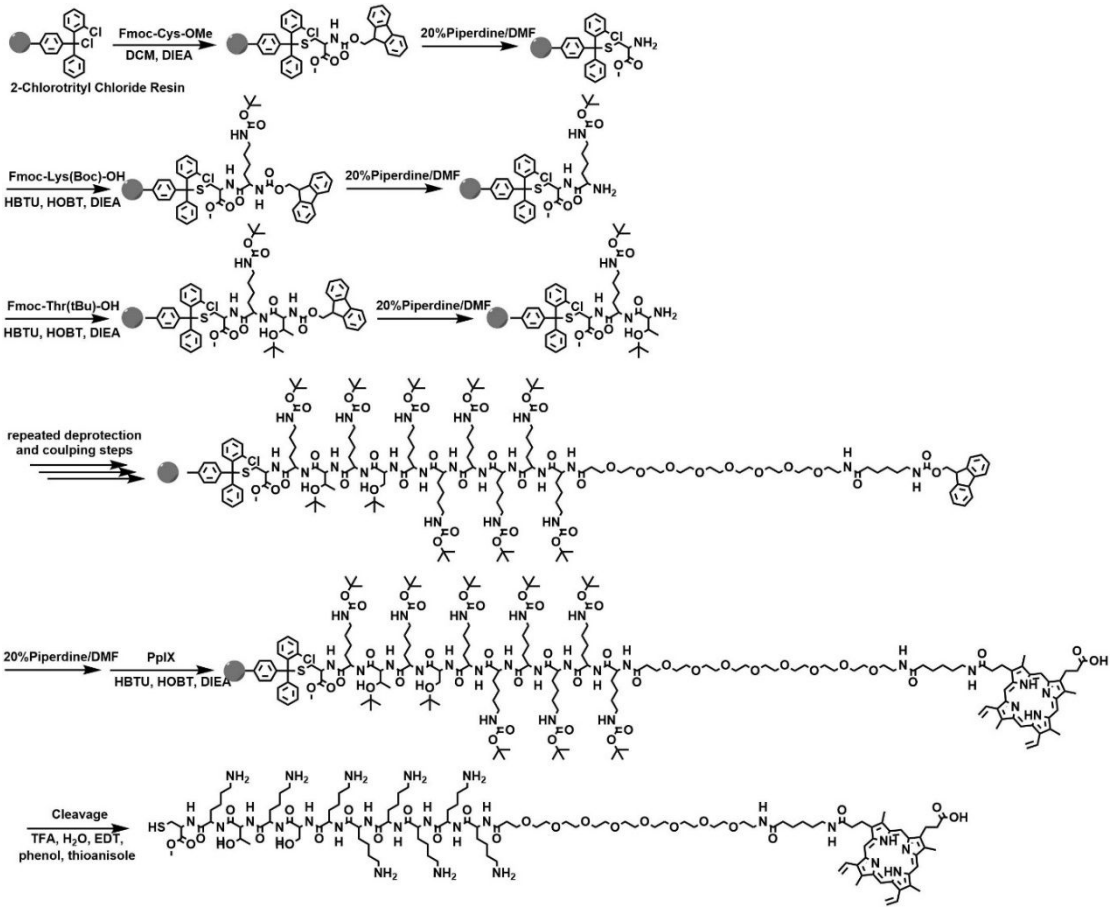

Figure S1. Synthesis route of the chimeric peptide PCPK.

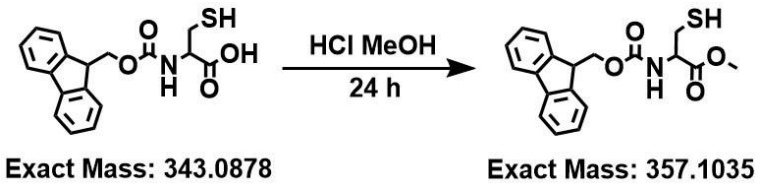

Figure S2. Synthesis procedure of Fmoc-Cys-OMe.

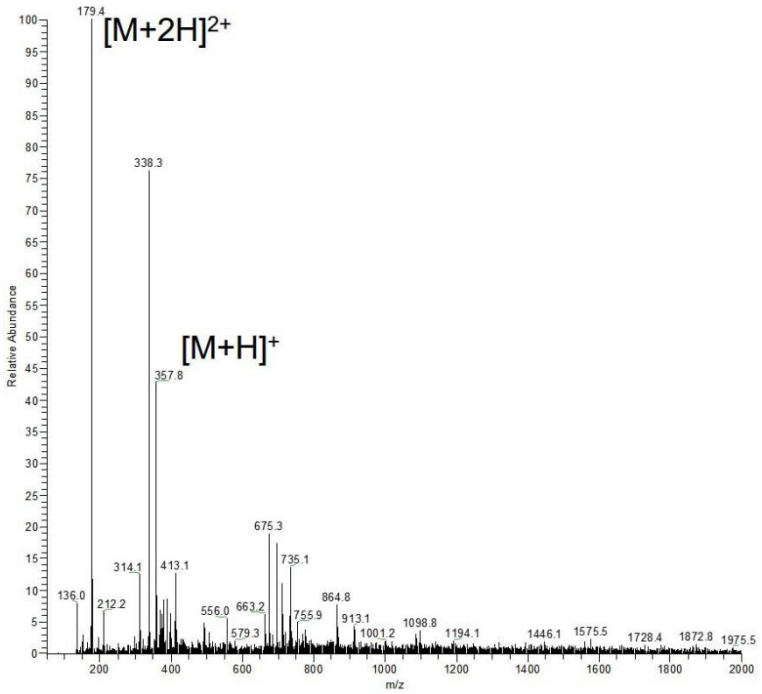

Figure S3. ESI-MS of Fmoc-Cys-OMe.

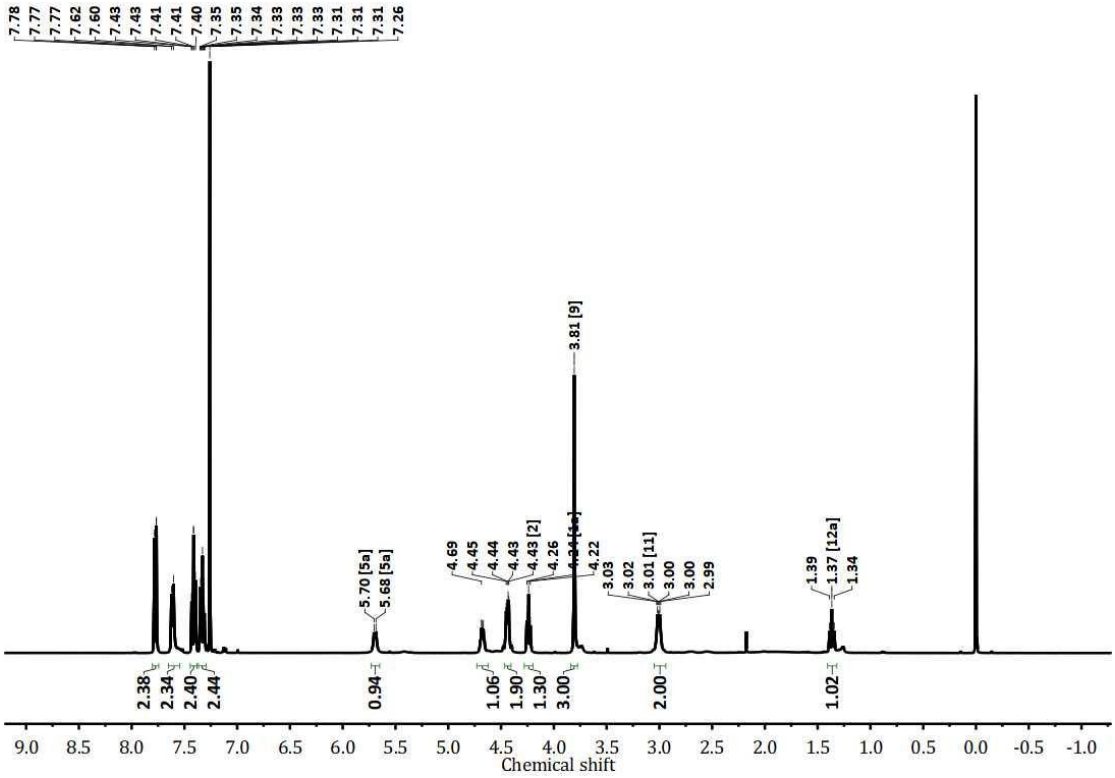

Figure S4. ^{1}H NMR of Fmoc-Cys-OMe.

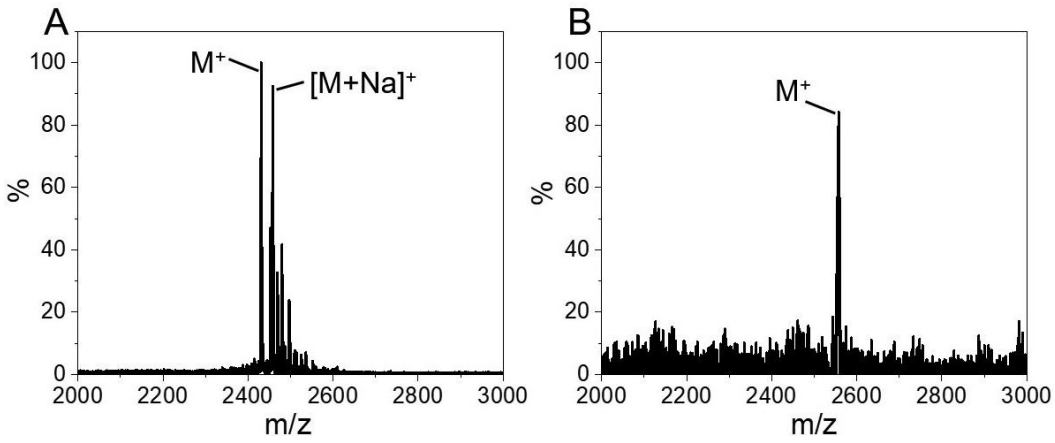

Figure S5. MALDI-TOF/MS of the chimeric peptide (A) PCPK and (B) PCPK-SR.

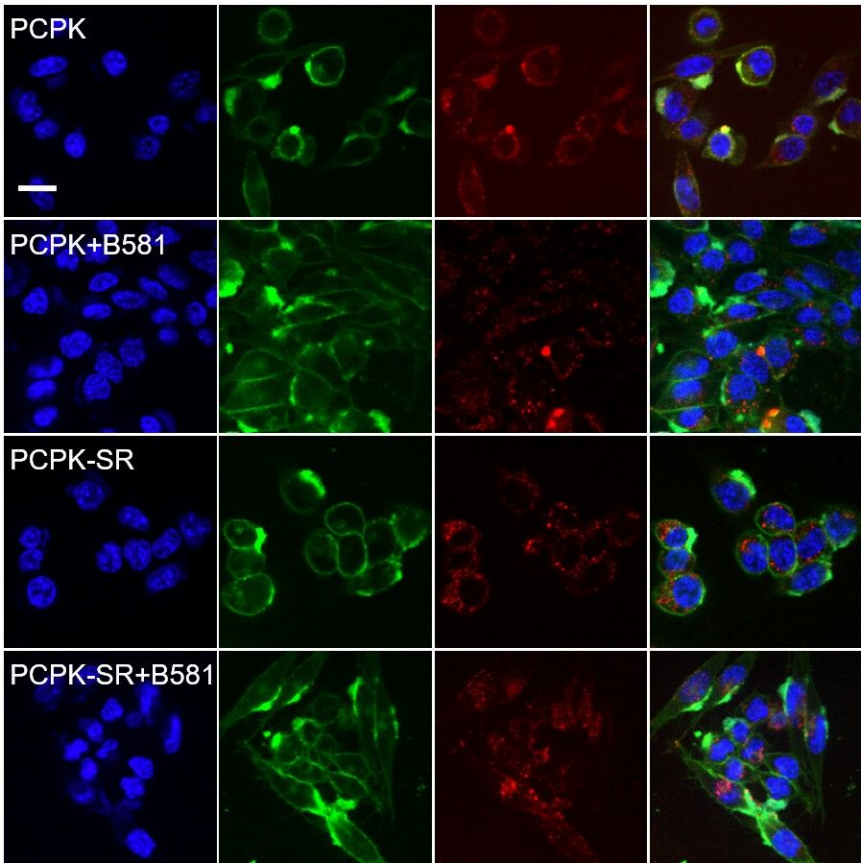

Figure S6. Confocal microscopic images of LLC cells pretreated with or without the PFTase inhibitor B581 and then incubated with PCPK and PCPK-SR. The cell nuclei (blue) and plasma membrane (green) were stained with Hoechst 33342 and CellMask green plasma membrane stain, respectively. The red fluorescence is from PpIX of the chimeric peptide PCPK and PCPK-SR. Scale bar: 20 μm.

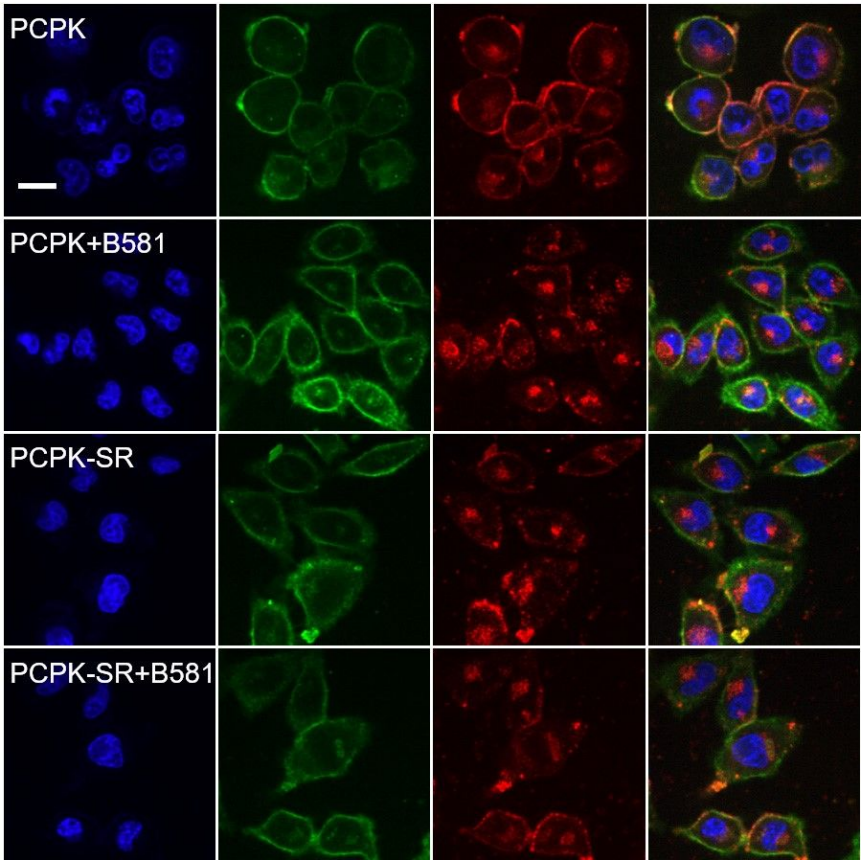

Figure S7. Confocal microscopic images of MCF-7 cells pretreated with or without the PFTase inhibitor B581 and then incubated with PCPK and PCPK-SR. The cell nuclei (blue) and plasma membrane (green) were stained with Hoechst 33342 and CellMask green plasma membrane stain, respectively. The red fluorescence is from PpIX of the chimeric peptide PCPK and PCPK-SR. Scale bar: 20 μm.

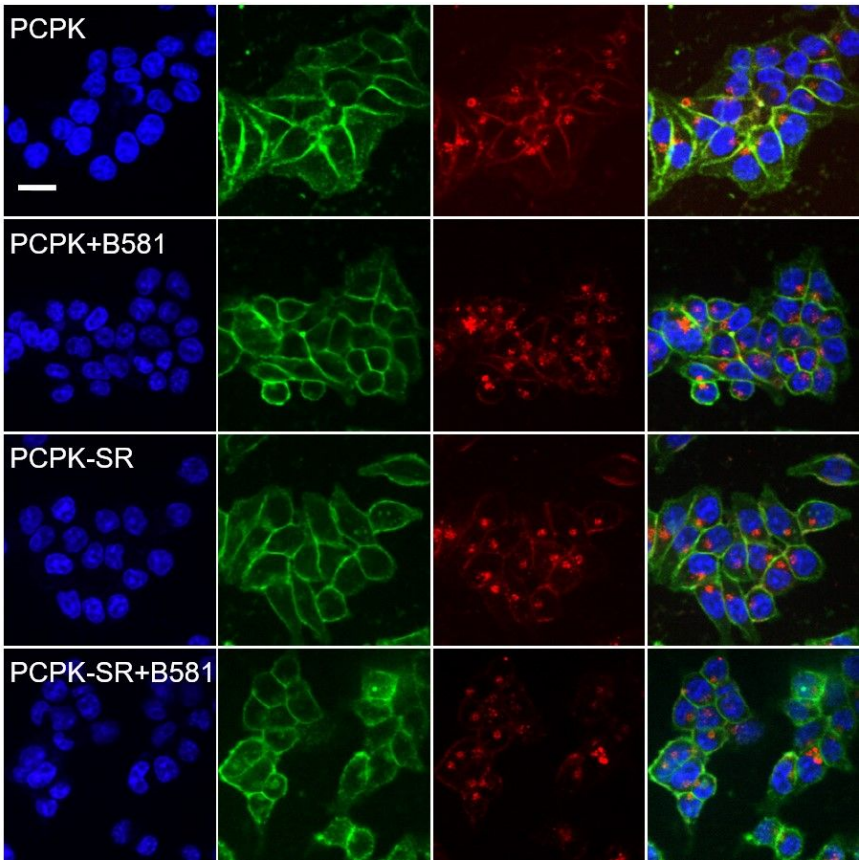

Figure S8. Confocal microscopic images of HCT-116 cells pretreated with or without the PFTase inhibitor B581 and then incubated with PCPK and PCPK-SR. The cell nuclei (blue) and plasma membrane (green) were stained with Hoechst 33342 and CellMask green plasma membrane stain, respectively. The red fluorescence is from PpIX of the chimeric peptide PCPK and PCPK-SR. Scale bar: 20 μm.

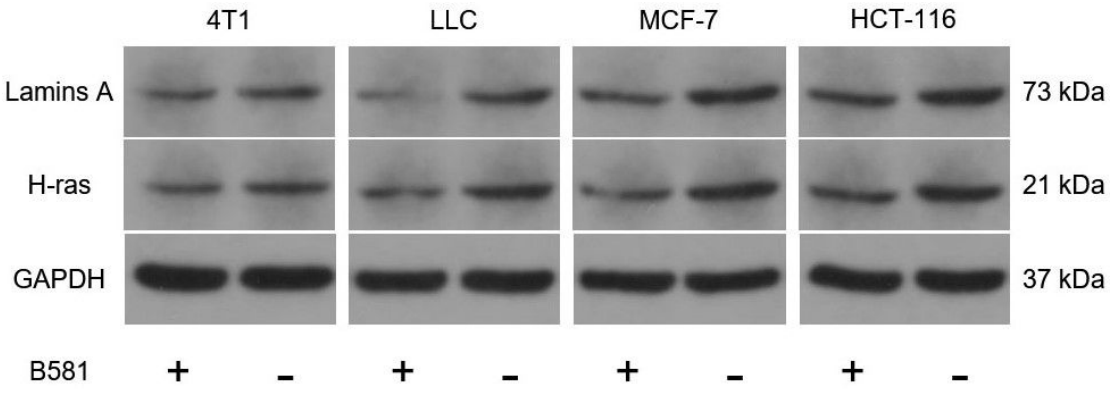

Figure S9. Western blotting analysis of H-Ras and lamins A among 4T1, LLC, MCF-7 and HCT-116 cells with and without pretreated with the PFTase inhibitor B581 for 12 h.

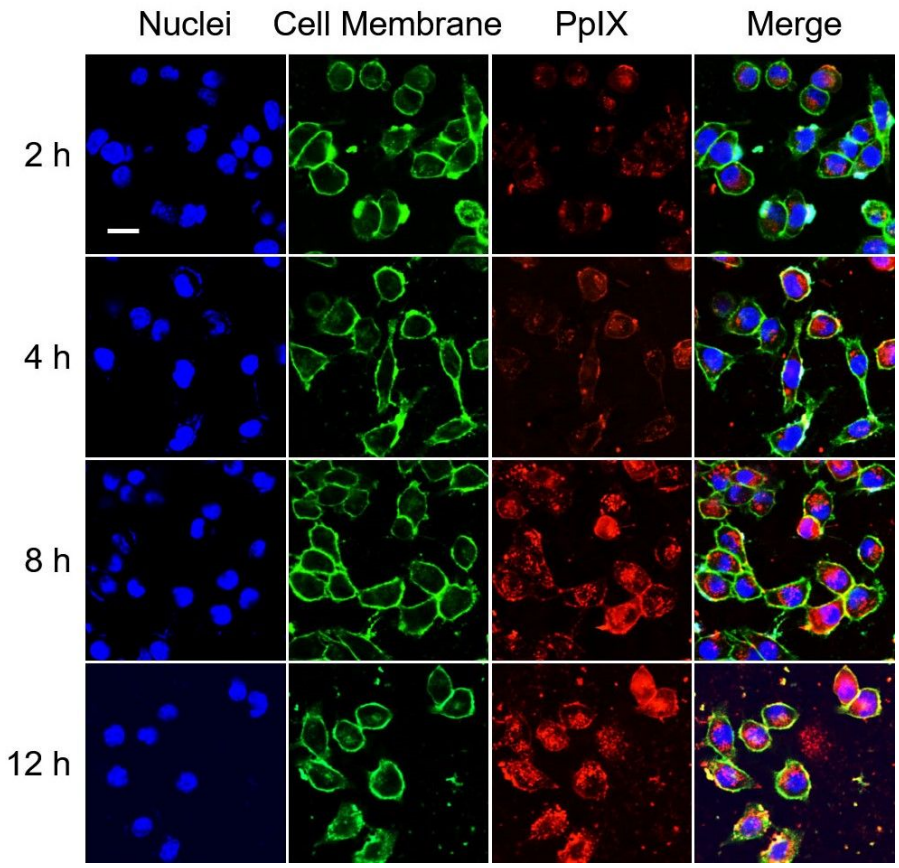

Figure S10. Confocal microscopic images of 4T1 cells treated with PCPK for 2 h, 4 h, 8 h and 12 h. The cell nuclei (blue) and plasma membrane (green) were stained with Hoechst 33342 and CellMask green plasma membrane stain, respectively. The red fluorescence is from PpIX of the chimeric peptide PCPK and PCPK-SR. Scale bar: 20 μm.

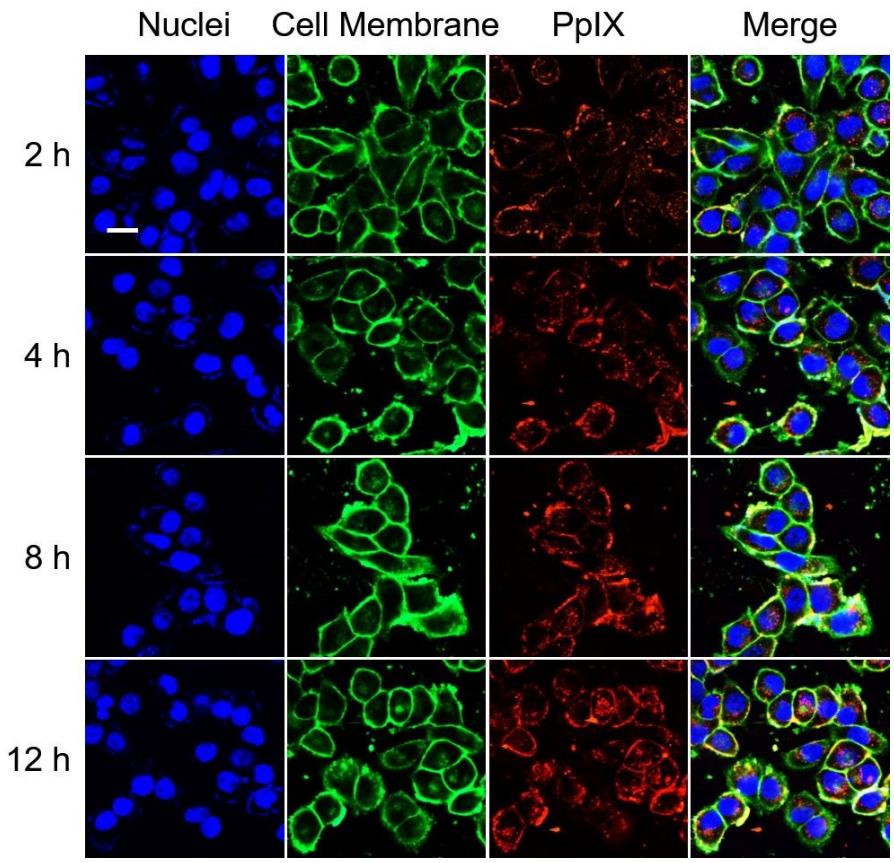

Figure S11. Confocal microscopic images of 4T1 cells treated with PCPK-SR for 2 h, 4 h, 8 h and 12 h. The cell nuclei (blue) and plasma membrane (green) were stained with Hoechst 33342 and CellMask green plasma membrane stain, respectively. The red fluorescence is from PpIX of the chimeric peptide PCPK and PCPK-SR. Scale bar: 20 μm.

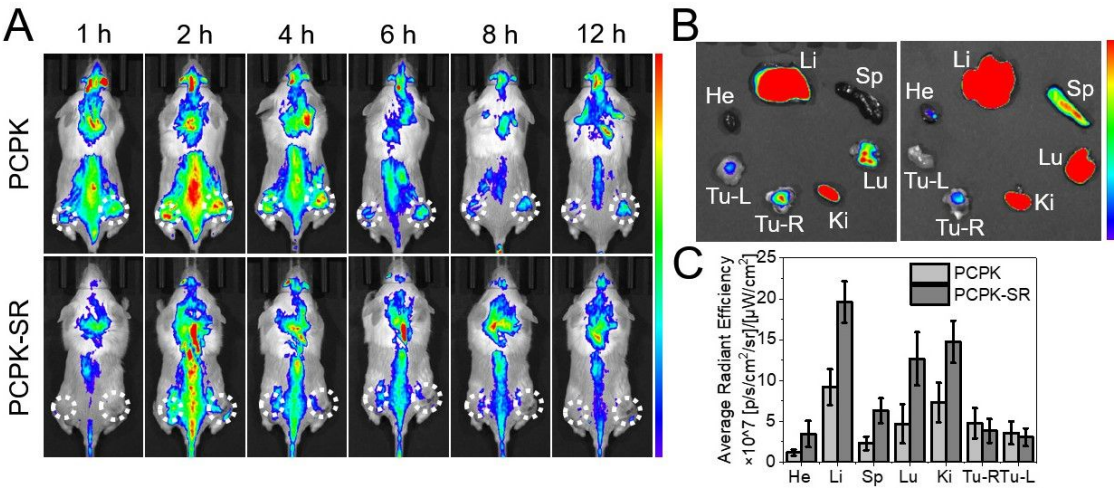

Figure S12. (A) *In vivo* fluorescence images of 4T1 tumor-bearing mice after intravenous injection of PCPK and PCPK-SR at different time intervals. The white circles indicate the 4T1 tumors. (B) *Ex vivo* fluorescence images and (C) the corresponding MFI values of various organs and tumor tissues at 12 h after intravenous injection. L indicates left and R indicates right.

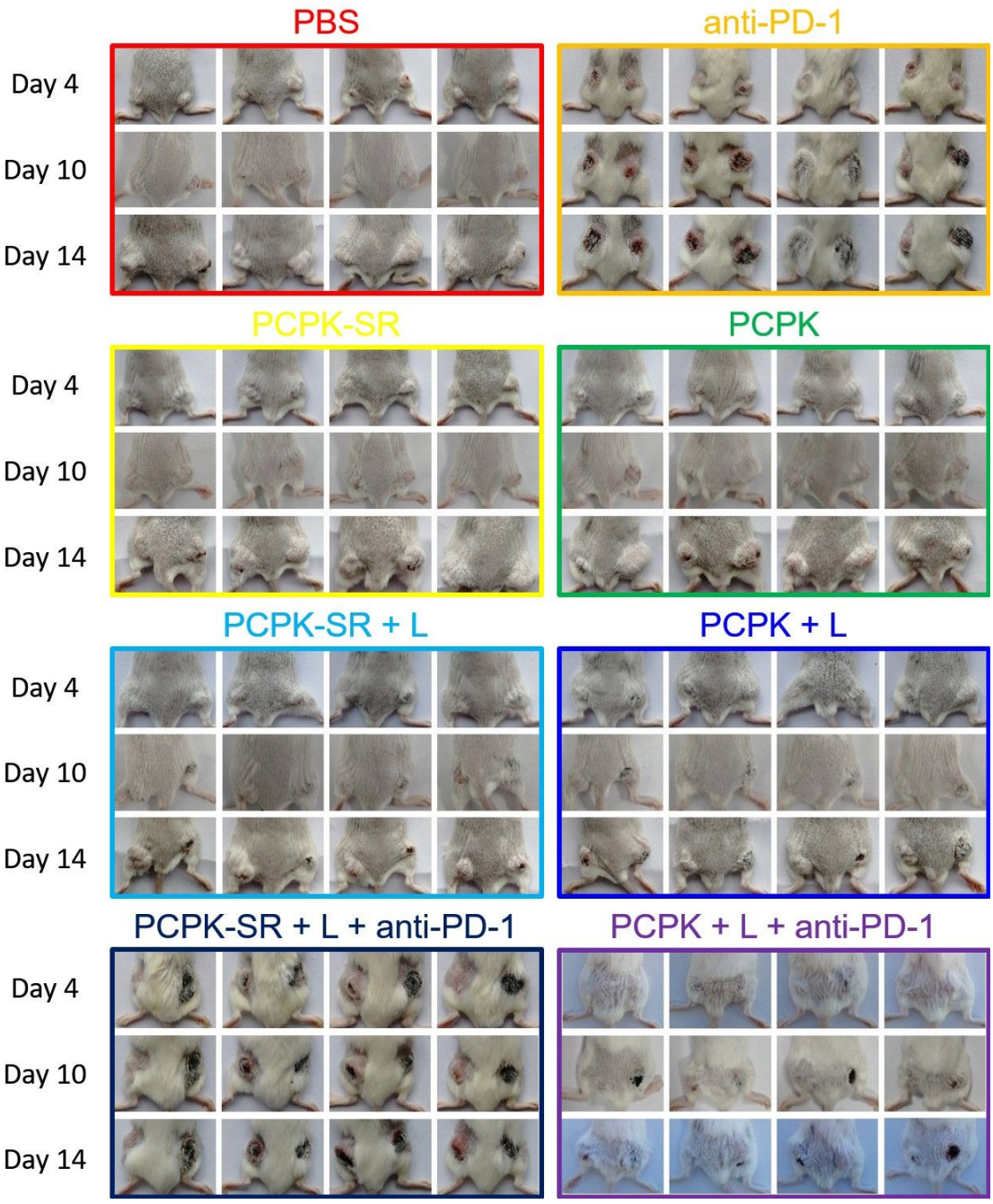

Figure S13. Photographs of 4T1 tumor-bearing mice with various treatments (PBS, anti-PD-1, PCPK-SR, PCPK, PCPK-SR+L, PCPK+L, PCPK-SR+anti-PD-1+L and PCPK+anti-PD-1+L) at different time points (4 d, 10 d and 14 d). L indicates 660 nm light irradiation (LED light, 30 mW cm^{-2}).

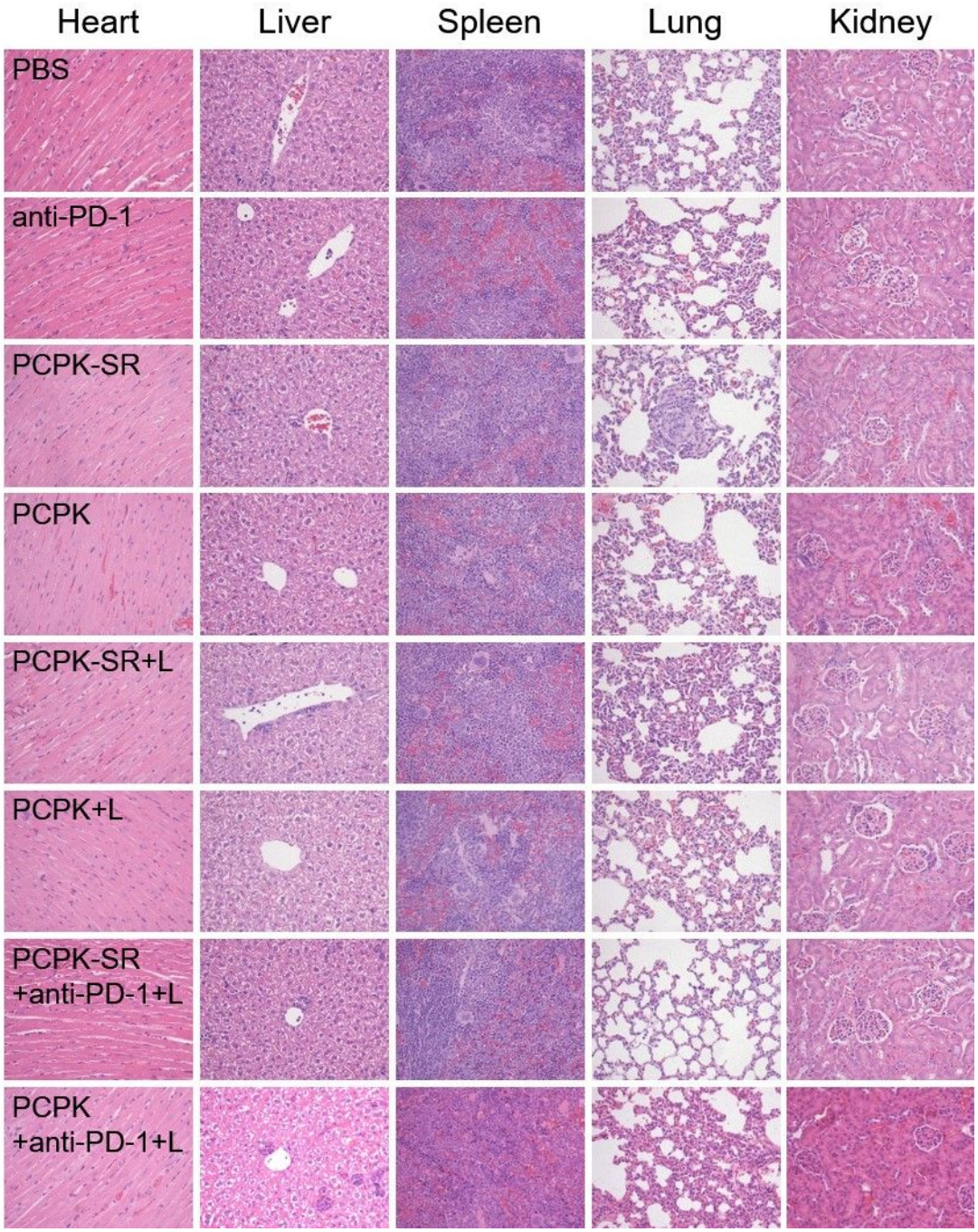

Figure S14. H&E-stained tissue sections from heart, liver, spleen, lung, and kidney organs of 4T1 tumor-bearing mice with various treatments (PBS, anti-PD-1, PCPK-SR, PCPK, PCPK-SR+L, PCPK+L, PCPK-SR+anti-PD-1+L and PCPK+anti-PD-1+L). L indicates 660 nm light irradiation (LED light, 30 mW cm^{-2}).

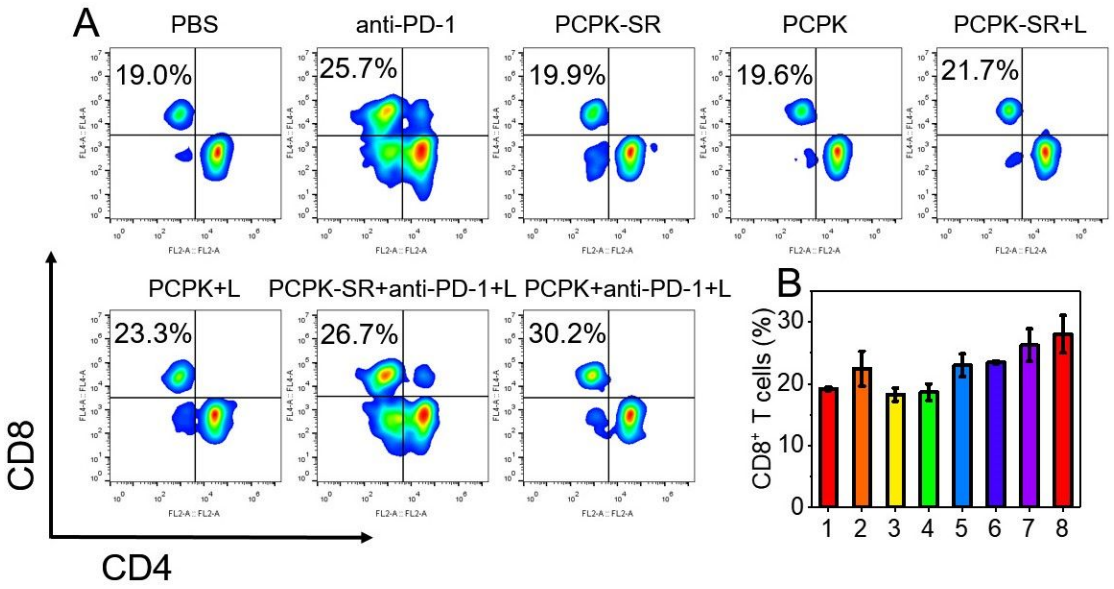

Figure S15. *In vivo* cytotoxic T lymphocytes ($CD8^+$) analysis in blood samples with various treatments: PBS (1), anti-PD-1 (2), PCPK-SR (3), PCPK (4), PCPK-SR+L (5), PCPK+L (6), PCPK-SR+anti-PD-1+L (7) and PCPK+anti-PD-1+L (8). L indicates 660 nm light irradiation (LED light, 30 mW cm^{-2}). (A) Cytotoxic T lymphocytes ($CD8^+$) in blood on 4T1 tumor-bearing mice with different treatments by FACS assay (gated by $CD3^+$). (B) Quantitative analysis of cytotoxic T lymphocytes in blood with different treatments.