

## Supporting Information

for *Adv. Sci.*, DOI 10.1002/advs.202203742

Multifunctional Protein Hybrid Nanoplatfom for Synergetic Photodynamic-Chemotherapy of Malignant Carcinoma by Homologous Targeting Combined with Oxygen Transport

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# Supporting Information

## **A Multifunctional Nanoplatfrom Based on Protein Hybrid for Enhancing Synergetic Photodynamic-Chemo Therapy Effect by Homologous Targeting Combined with Oxygen Transport**

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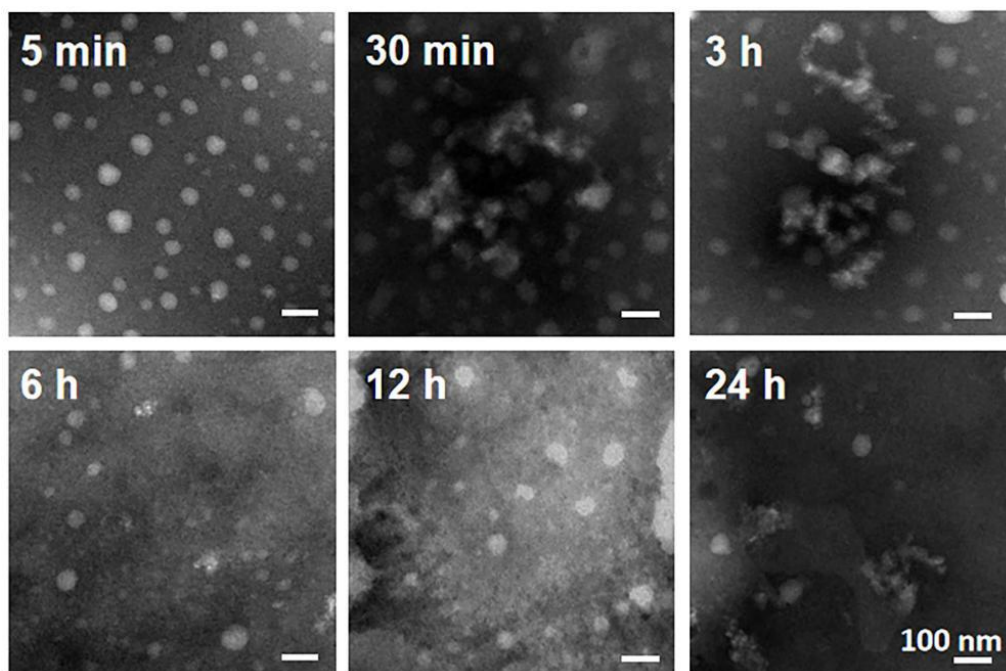
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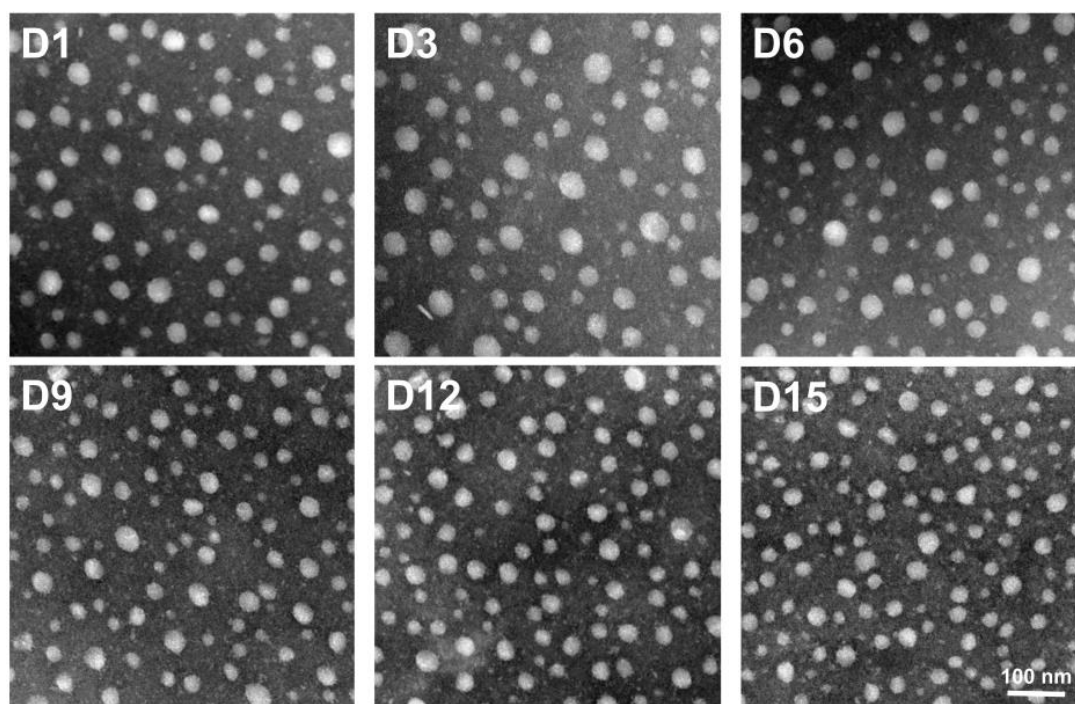
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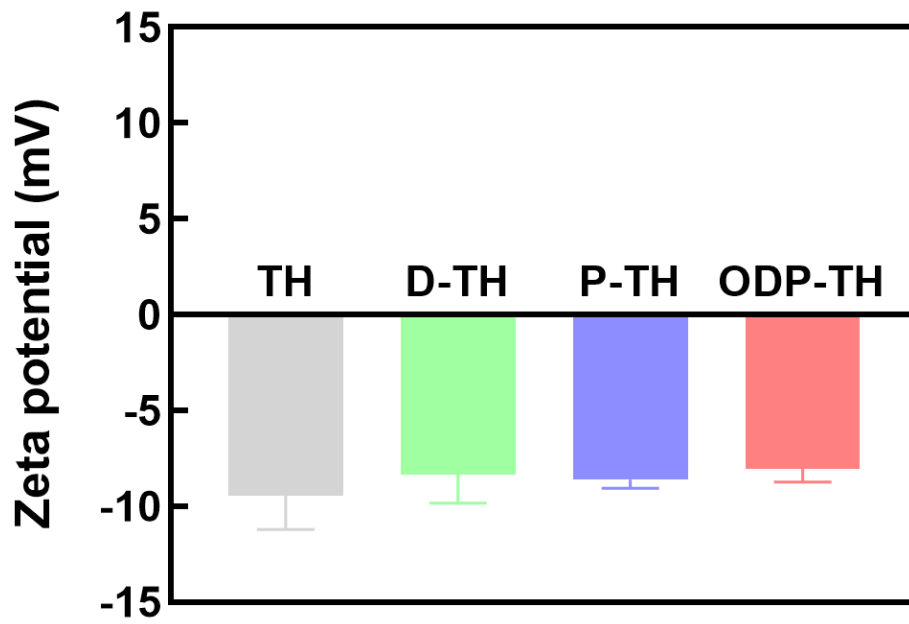
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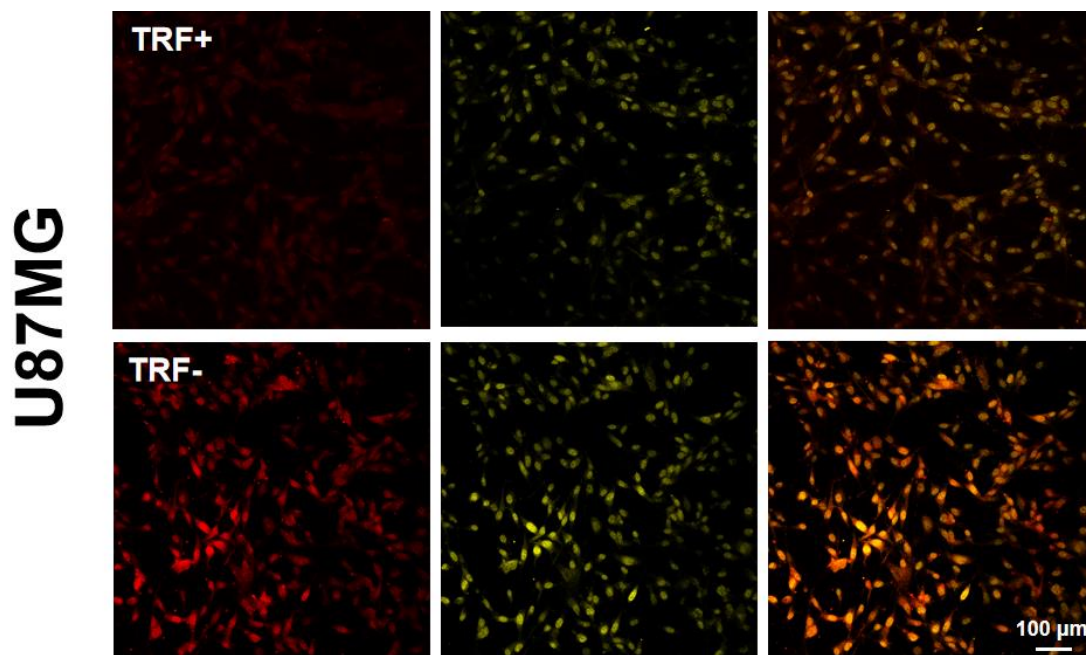
**Figure S1.** TEM of ODP-TH incubated with GSH (5 mM) in PBS at 25 °C from 5 min to 24 h. Scale bar = 100  $\mu\text{m}$ .



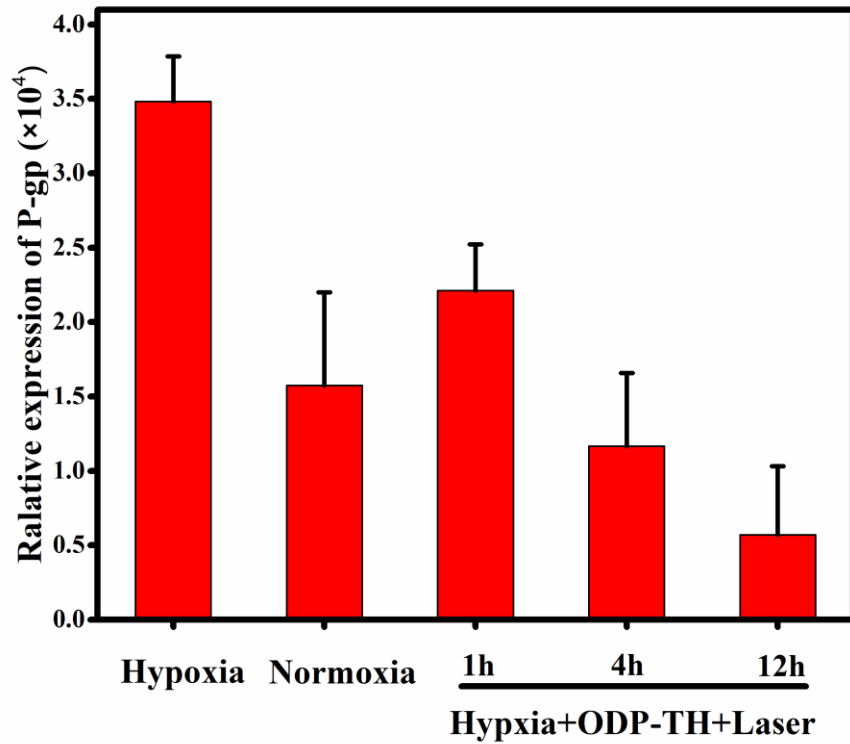
**Figure S2.** The TEM images of ODP-TH dispersed in PBS on D1, D3, D6, D9, D12, D15 at 25 °C. Scale bar = 100  $\mu\text{m}$ .



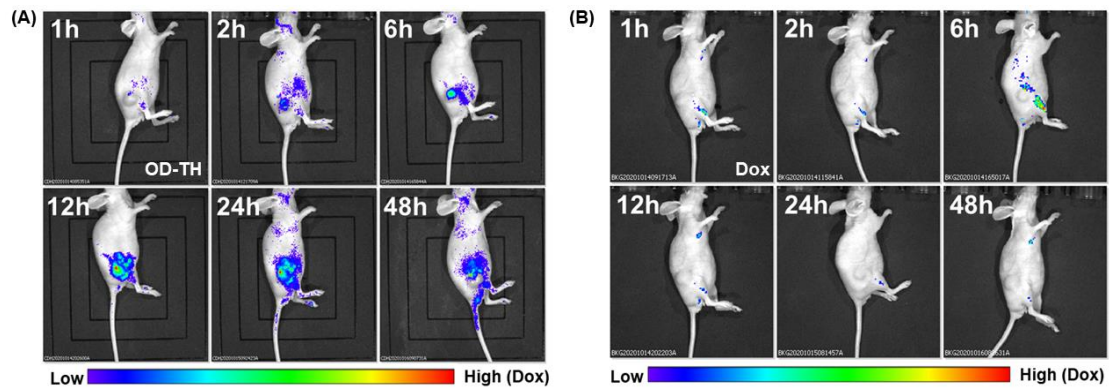
**Figure S3.** Zeta potential of TH nanoshell, single loaded D-TH and P-TH, dual loaded ODP-TH. Mean  $\pm$  SD, n = 3.



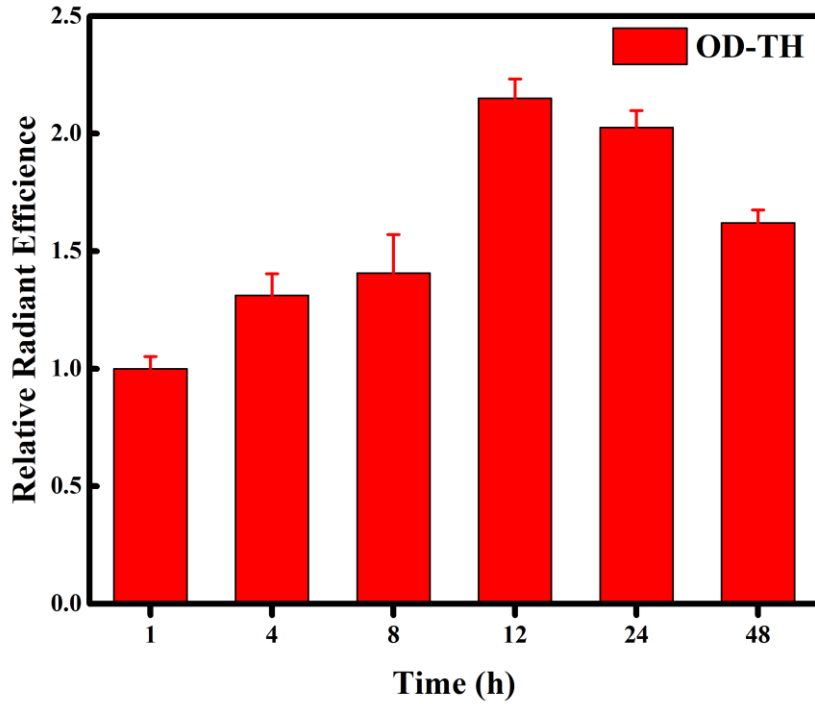
**Figure S4.** CLSM images of ODP-TH uptake in U87MG cells treated with TRF (500  $\mu$ M) for 4 h and untreated U87MG cells. Scale bar = 100  $\mu$ m



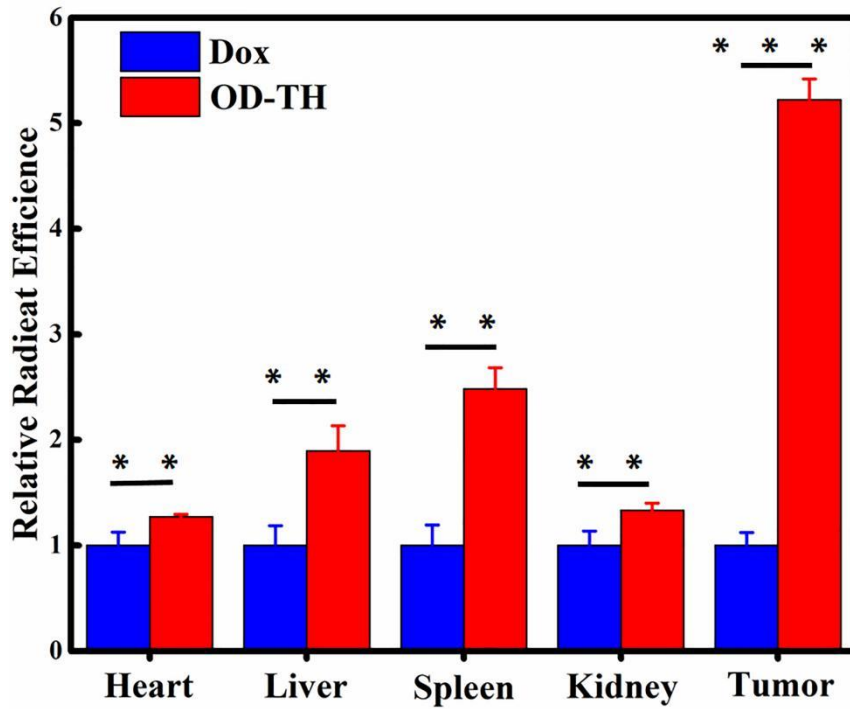
**Figure S5.** Semi-quantitative analysis of P-gp expression of 4T1 cells in different state. Mean  $\pm$  SD, n = 3.



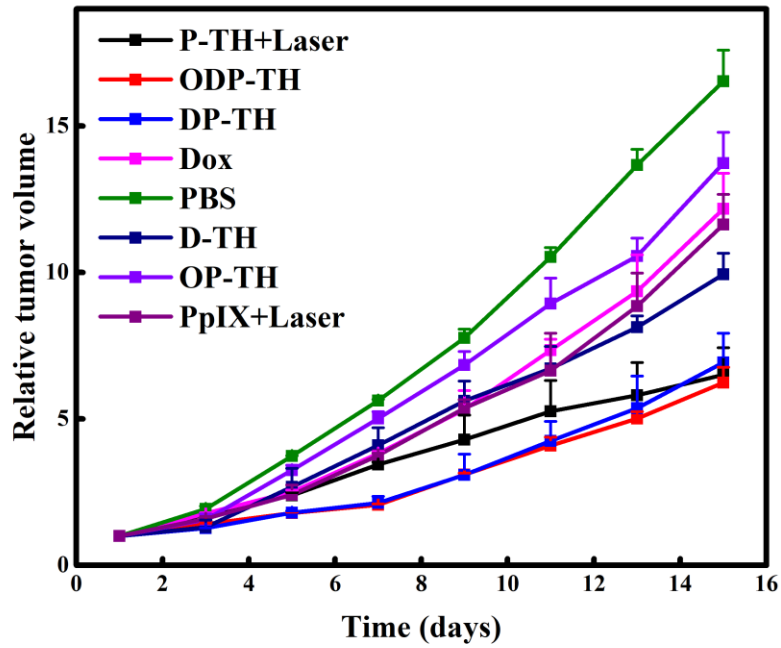
**Figure S6.** Time lapse fluorescence image of 4T1 tumor bearing BALB/c nu mice after injection of OD-TH (A) and Dox (B).



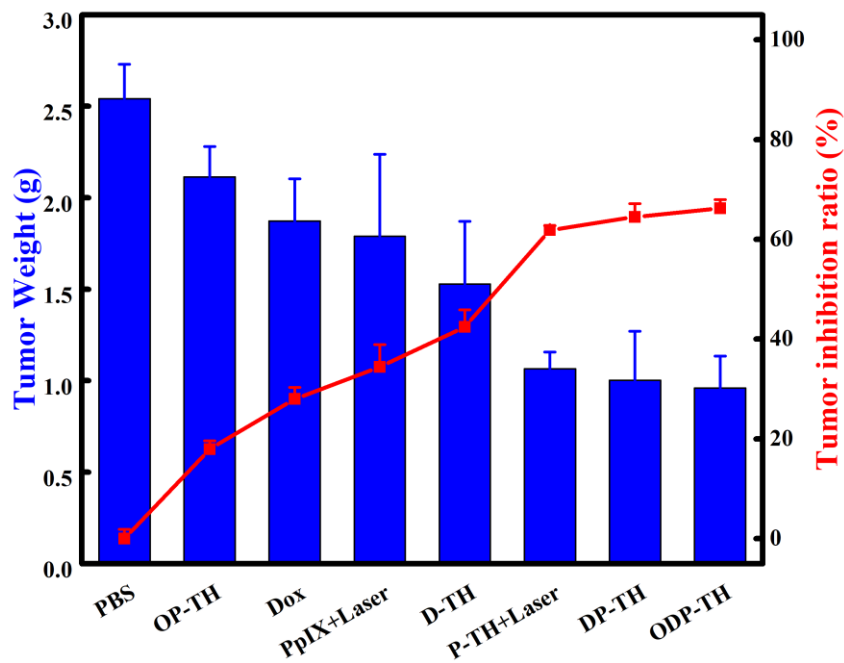
**Figure S7.** Semi-quantitative analysis of radiant efficiency in ODP-TH treated mice tumour region at different time. All data were analyzed by software (imageJ). Mean  $\pm$  SD, n = 3.



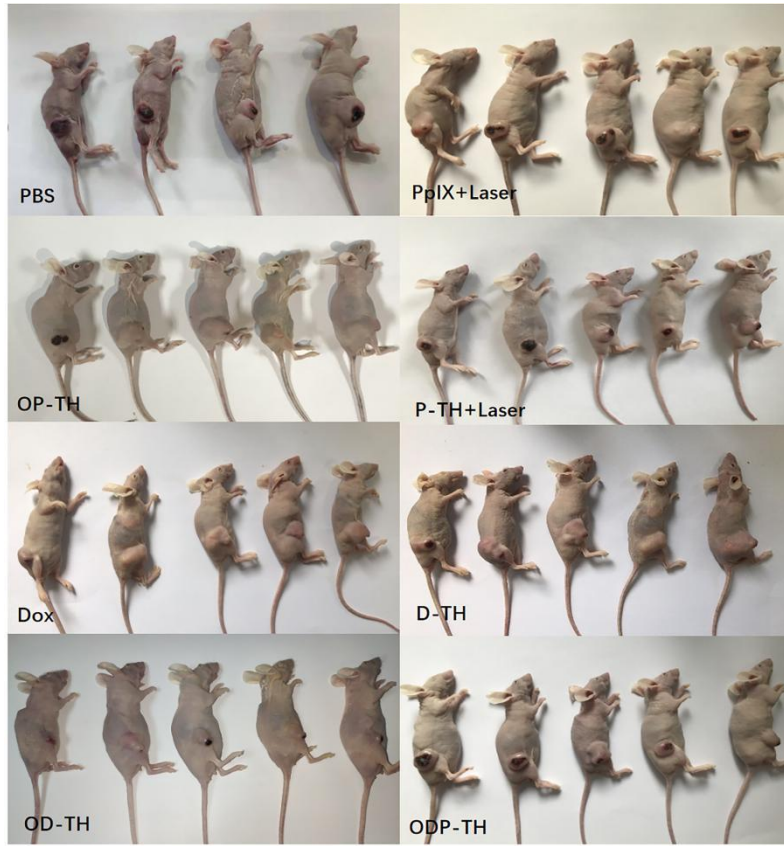
**Figure S8.** Relative fluorescence histogram of major organs and tumor 48 h after tail vein injection of Dox and OD-TH. Mean  $\pm$  SD, n = 3. *P*-value were indicated by \*\* ( $p < 0.01$ ) and \*\*\* ( $p < 0.001$ ).



**Figure S9.** 4T1 tumor volume changes curves of different groups within 15 days after administration. Mean  $\pm$  SD, n = 5.

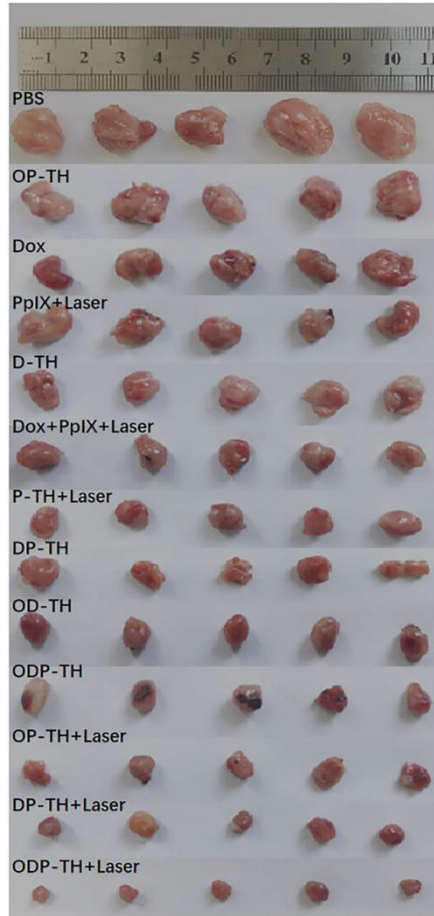


**Figure S10.** Tumor weight and inhibition rate in mice after 15 days after treatment. Mean  $\pm$  SD, n = 5.

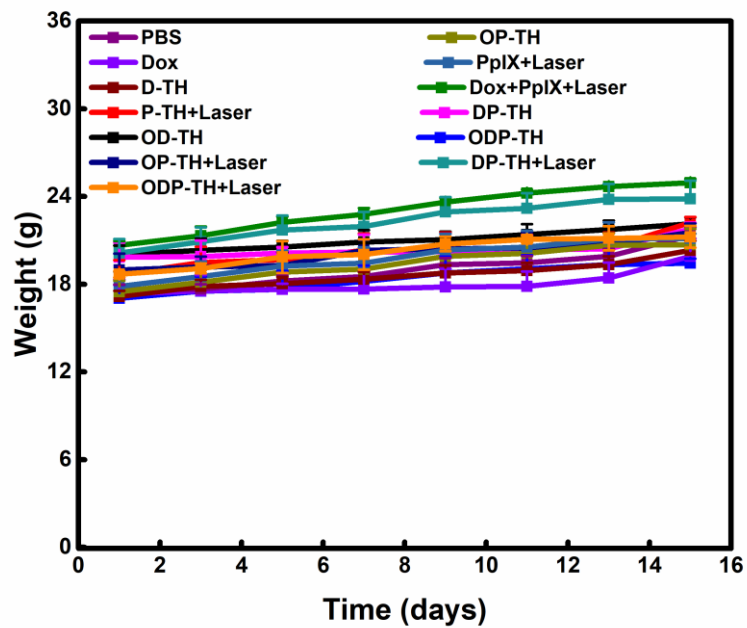


**Figure S11.** Pictures of mice at termination of treatment in eight groups.

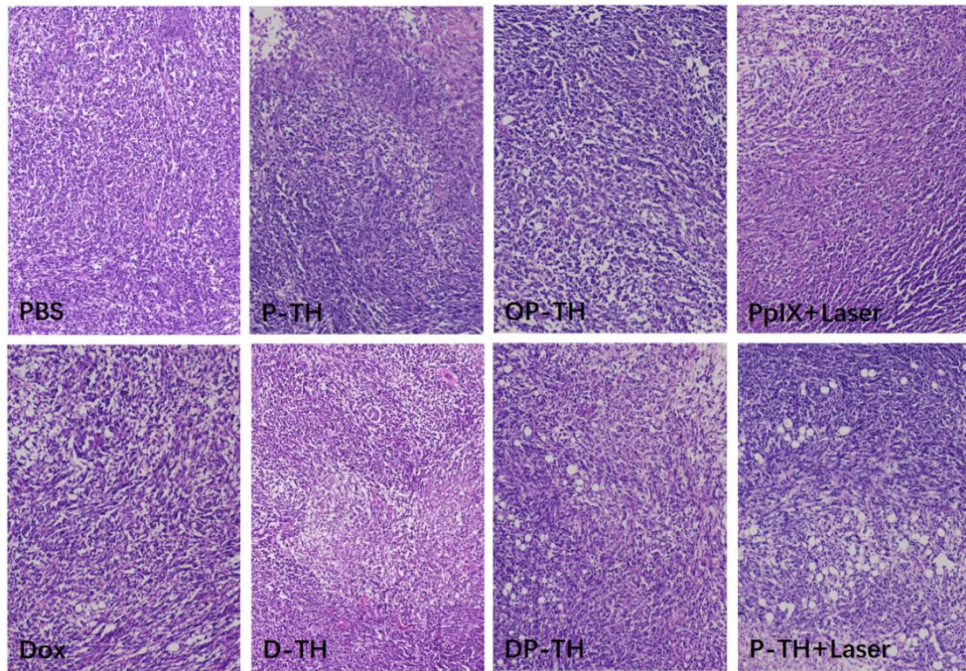




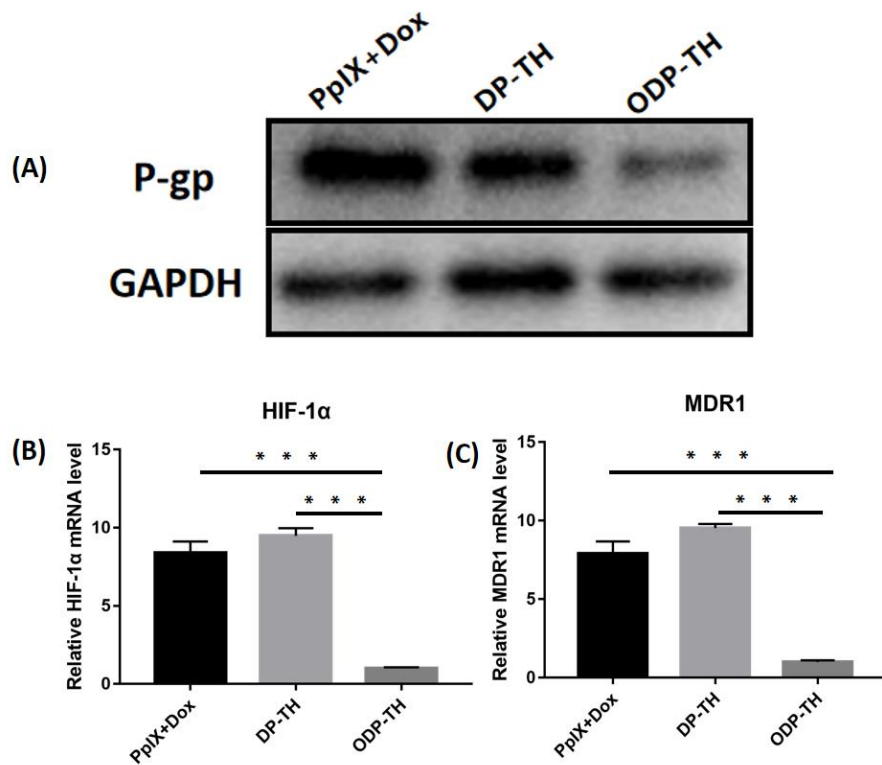
**Figure S12.** Images of all mice at the termination of treatment and tumor dissection.



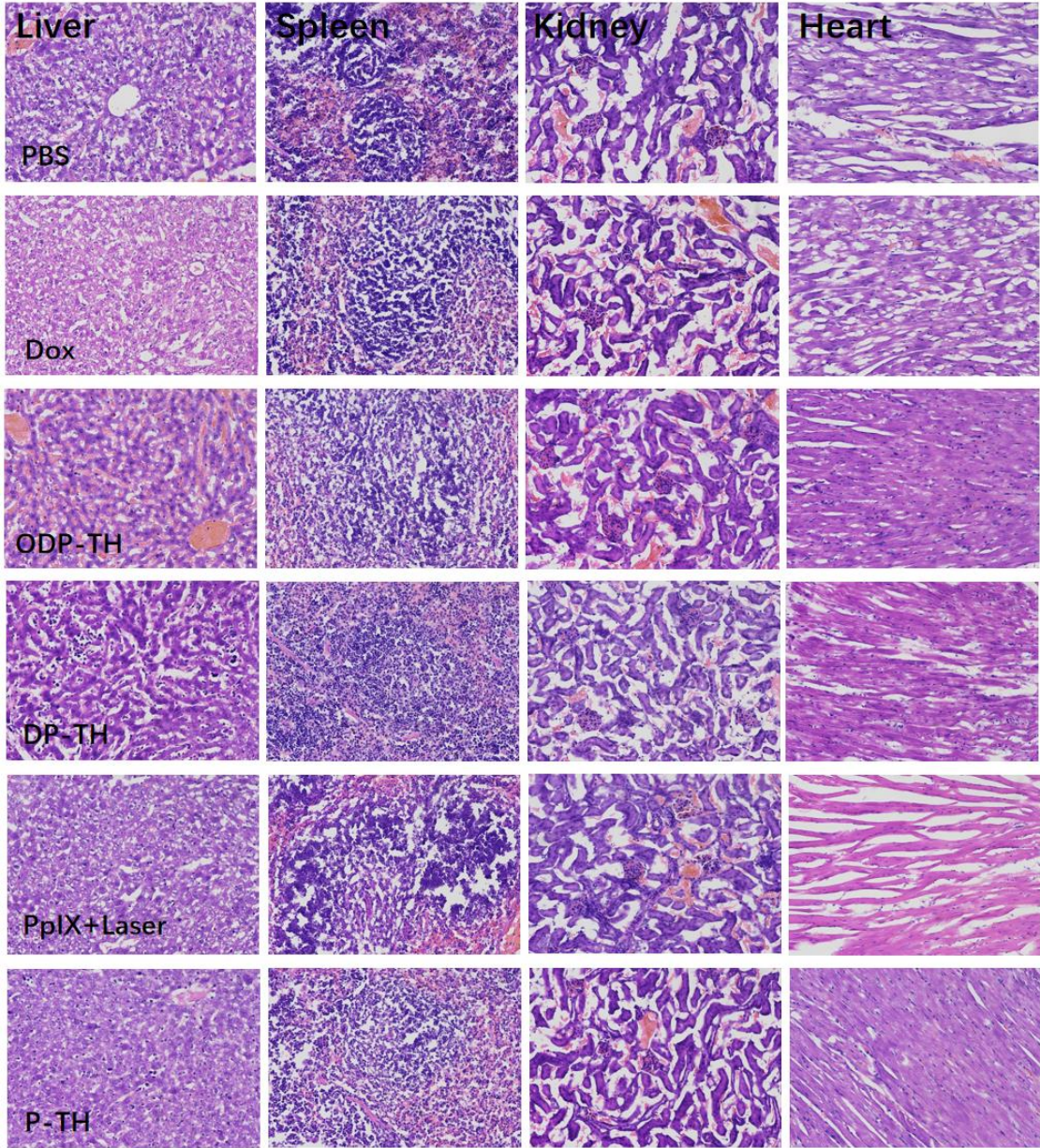
**Figure S13.** Weight change curves of all mice during treatment. Mean  $\pm$  SD, n = 5.

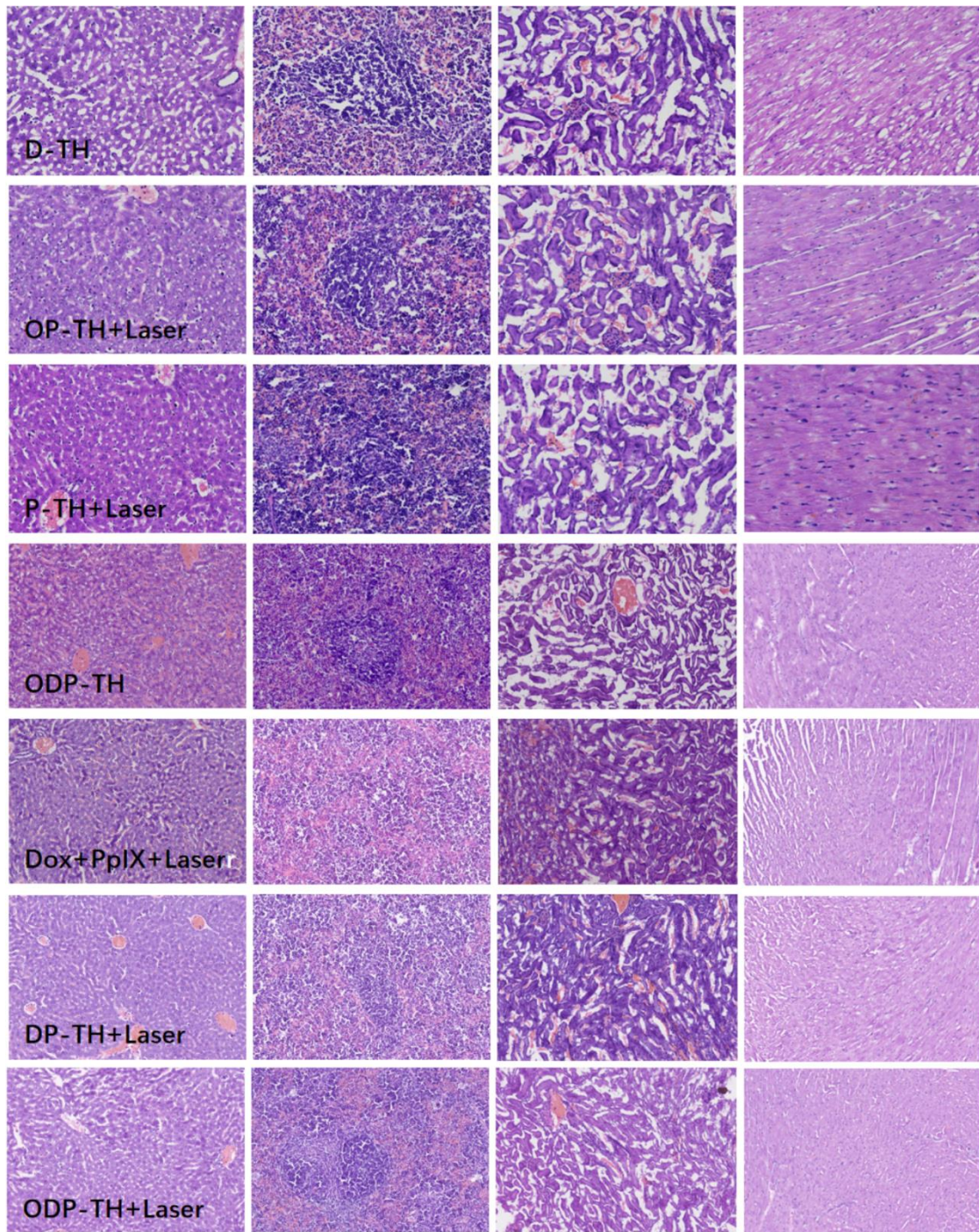


**Figure S14.** H&E staining images for the dissected tumors in seven groups. (100x)

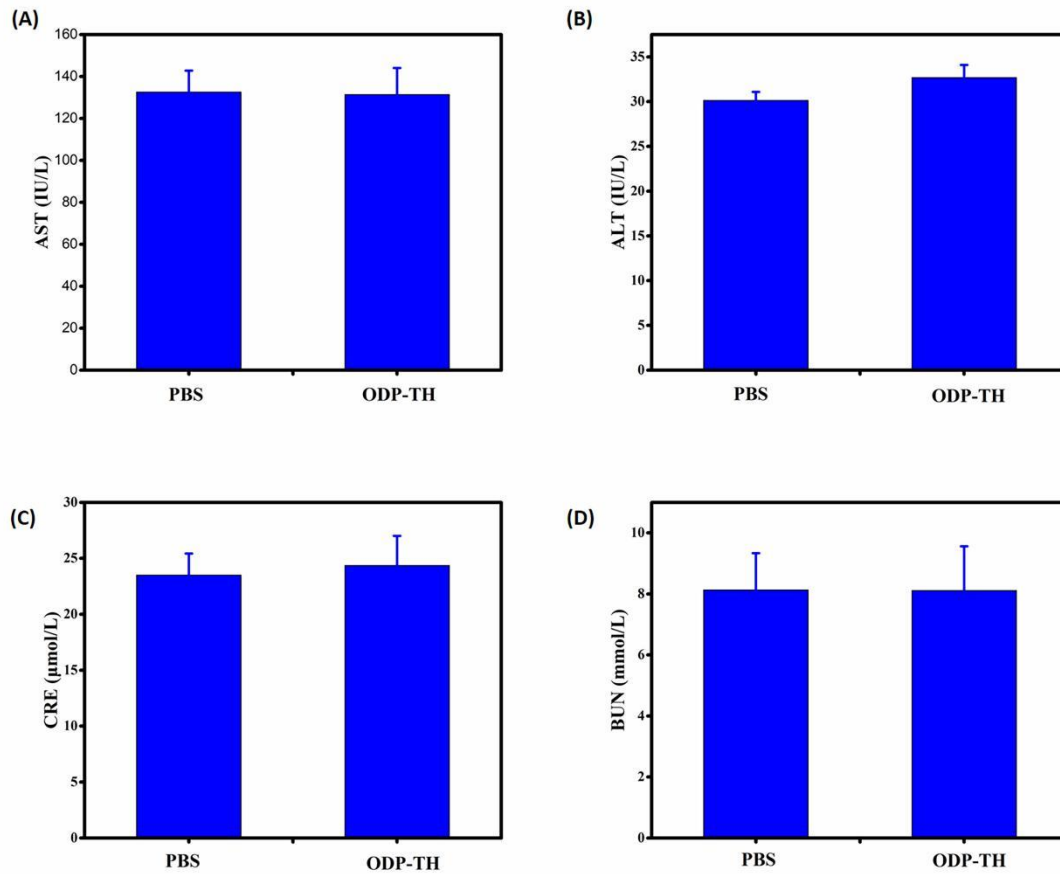


**Figure S15.** WB and qRT-PCR analysis of P-gp (A), HIF-1 $\alpha$  (B) and MDR1 (C) expression of 4T1 tumor tissues treated with PpIX + Dox, DP-TH and ODP-TH for 12 h. Mean  $\pm$  SD,  $n = 3$ .  $P$ -value were indicated by \*\*\* ( $p < 0.001$ ).

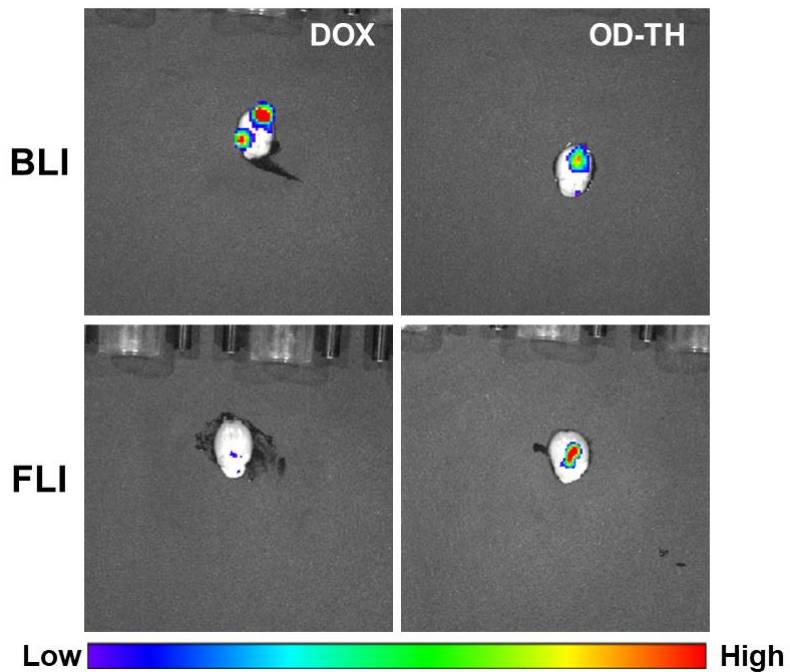




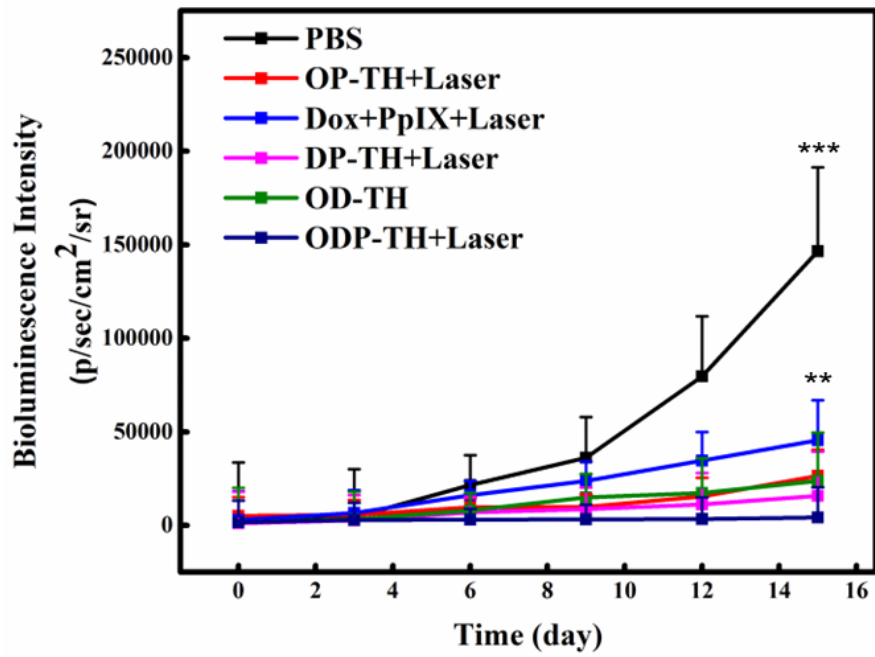
**Figure S16.** H&E staining images for the dissected major organs in 4T1 cells bearing mice. (200x)



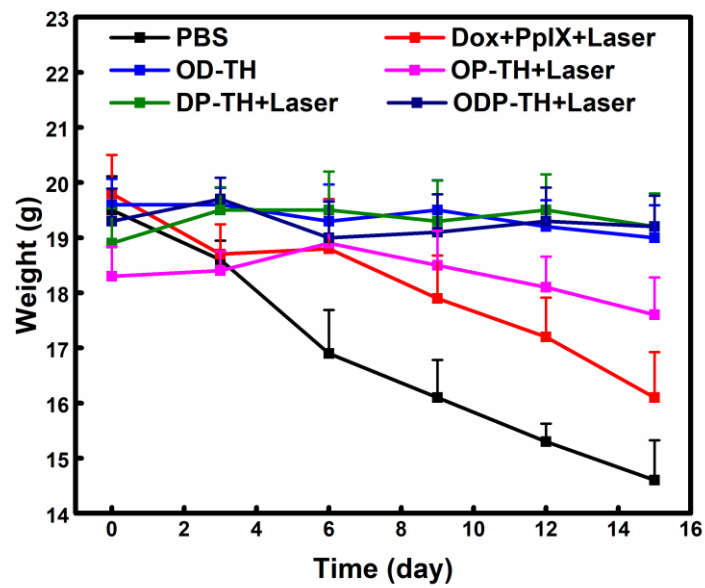
**Figure S17.** Detection of physiological indexes in blood of ODP-TH administrated mice. Mean  $\pm$  SD, n = 3.



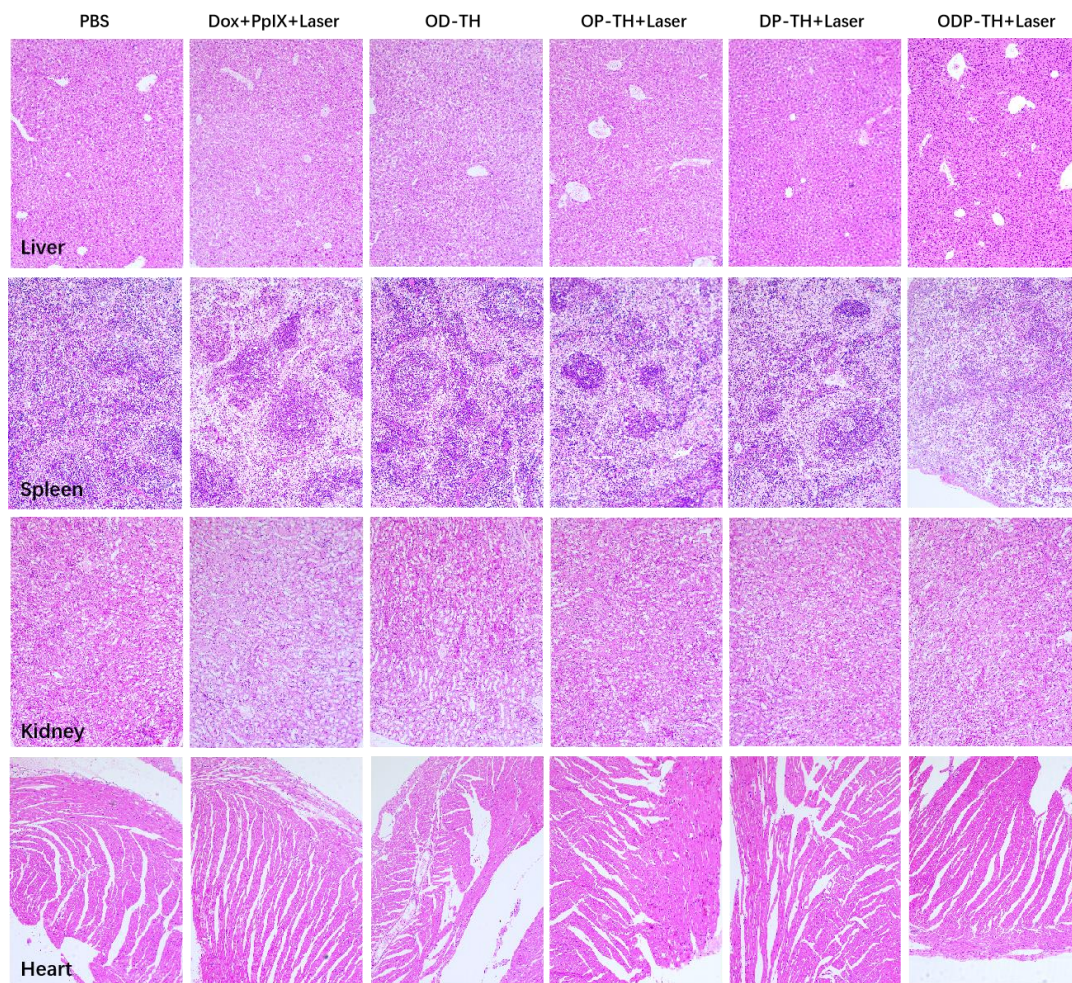
**Figure S18.** Imaging of bioluminescence (BLI) and fluorescence (FLI) co-localization in isolated brain tissue after 48 h treatment.



**Figure S19.** The brain BLI change curve of U87MG orthotopic transplanted mice. Mean  $\pm$  SD, n = 3.



**Figure S20.** The weight change curve of U87MG orthotopic transplanted mice. Mean  $\pm$  SD, n = 3.



**Figure S21.** H&E staining images for the dissected major organs in U87MG cells bearing mice. (100x)