

## **Supplementary Information**

### **Mitochondria-Targeted Nanospheres with Deep Tumor Penetration for Photo/Starvation Therapy**

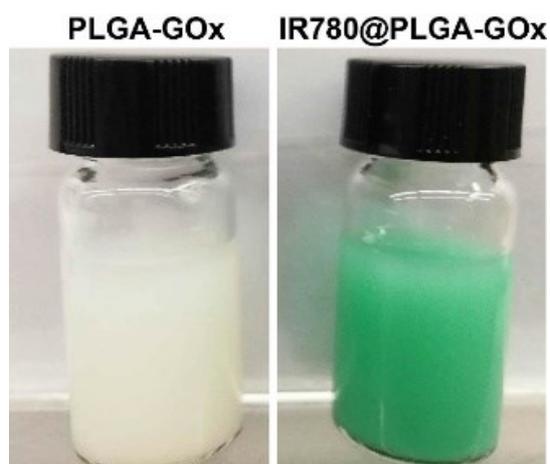
Yong Wang,<sup>‡, a</sup> Bo Wang,<sup>‡, a</sup> Liang Zhang,<sup>‡, b</sup> Ju Huang,<sup>b</sup> Pan Li,<sup>b</sup> Yahui  
Zhao,<sup>c</sup> Chen Zhou,<sup>a</sup> Mei Liu,<sup>c</sup> Weiwei Li,<sup>c</sup> Jie He<sup>\*d</sup>

*<sup>a</sup>Department of Ultrasound, National Cancer Center, National Clinical Research Center for Cancer, Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100021, China.*

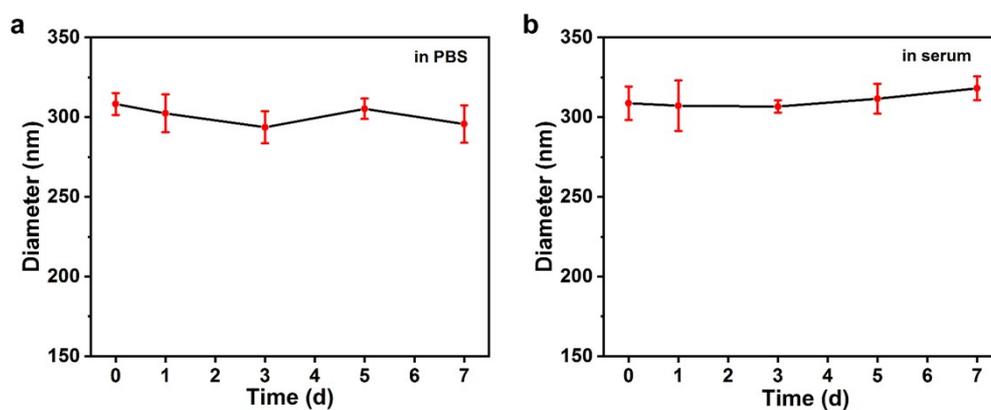
*<sup>b</sup>Department of Ultrasound, The Second Affiliated Hospital of Chongqing Medical University, Chongqing 400010, China.*

*<sup>c</sup>State Key Laboratory of Molecular Oncology, National Cancer Center, National Clinical Research Center for Cancer, Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100021, China.*

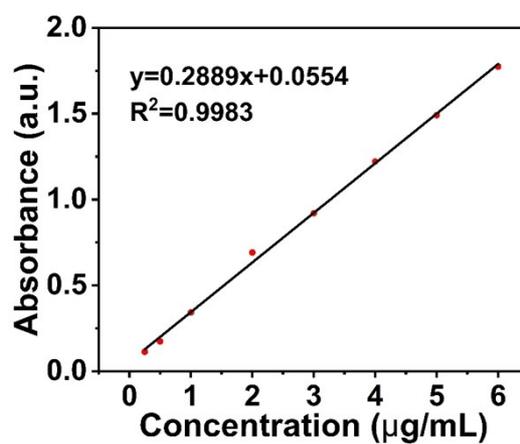
*<sup>d</sup>Department of Thoracic Surgery, National Cancer Center, National Clinical Research Center for Cancer, Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100021, China.*



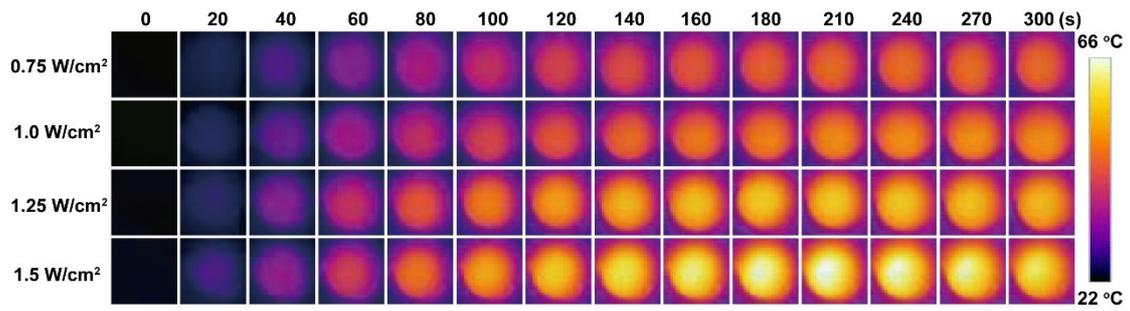
**Fig. S1** Digital photographs of PLGA-GOx and IR780@PLGA-GOx dispersed in PBS at concentrations of 10 mg/mL.



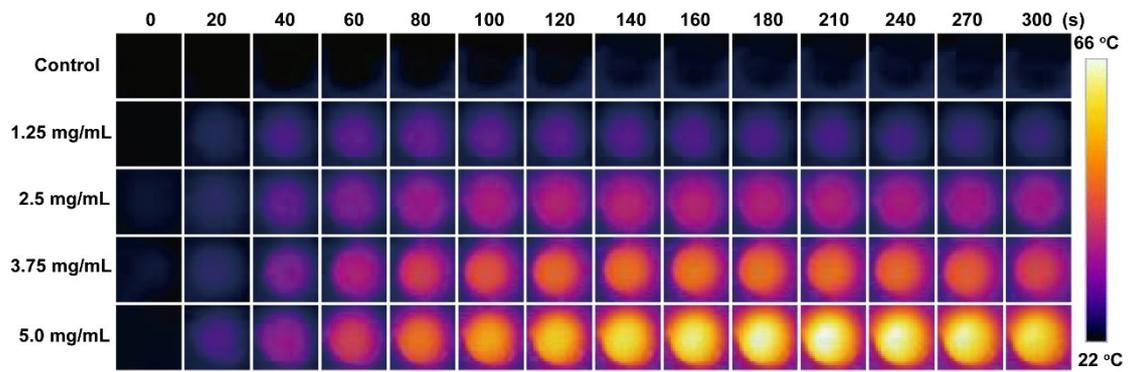
**Fig. S2** Stability analysis of IR780@PLGA-GOx nanoparticles in PBS (a) and in serum (b).



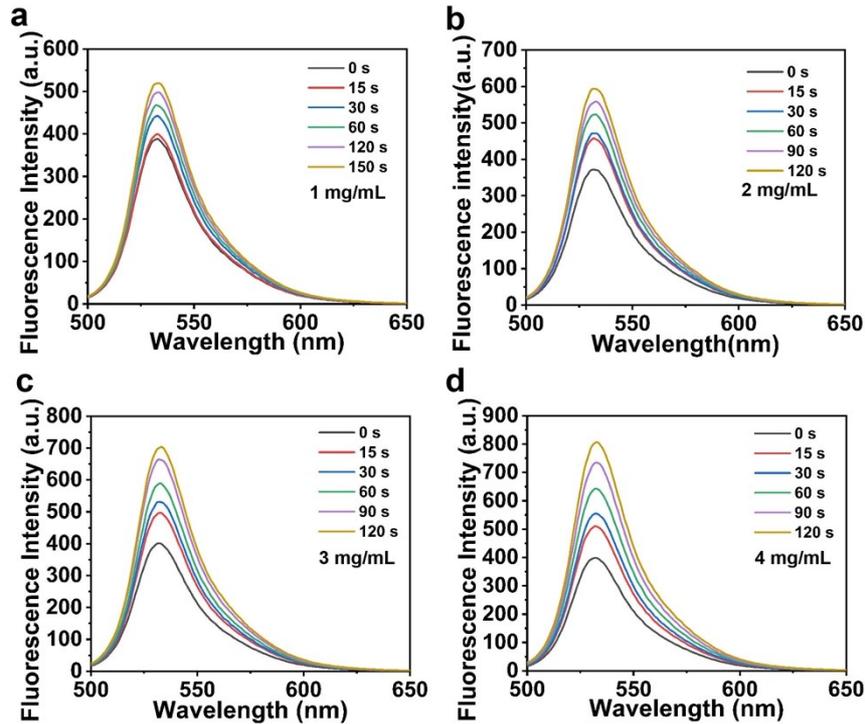
**Fig. S3** Relative absorbance intensity of IR780 in UV-vis spectrum at the wavelength of 783 nm.



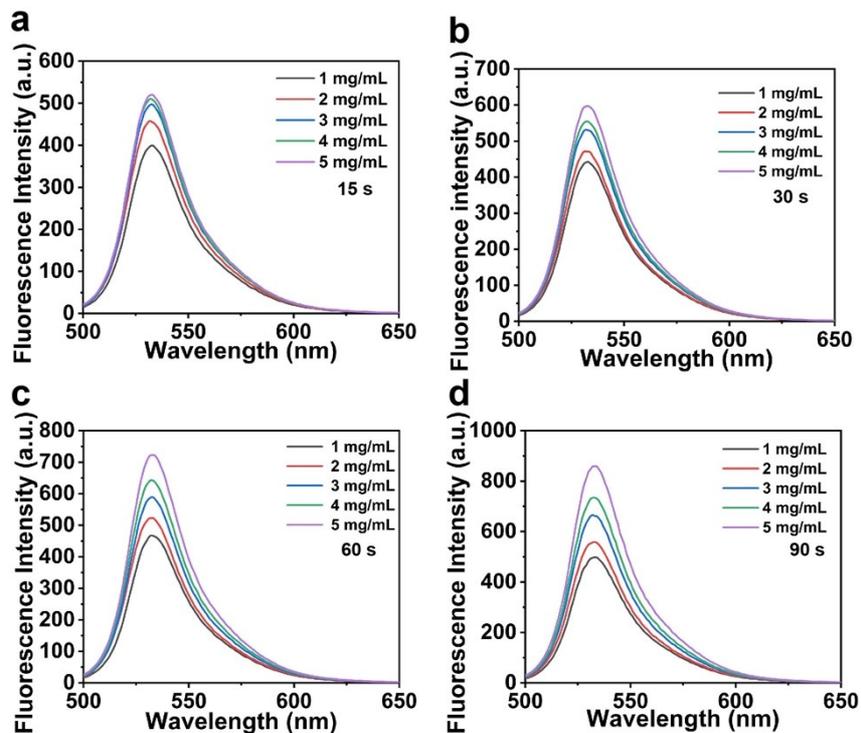
**Fig. S4** Infrared thermograms of IR780@PLGA-GOx suspensions irradiated with an 808 nm laser at different power intensities (0.75, 1.0, 1.25 and 1.5 W/cm<sup>2</sup>) and for various durations.



**Fig. S5** Infrared thermograms of IR780@PLGA-GOx suspensions at different concentrations (0, 1.25, 2.5, 3.75 and 5 mg/mL) irradiated with an 808 nm laser for various durations.

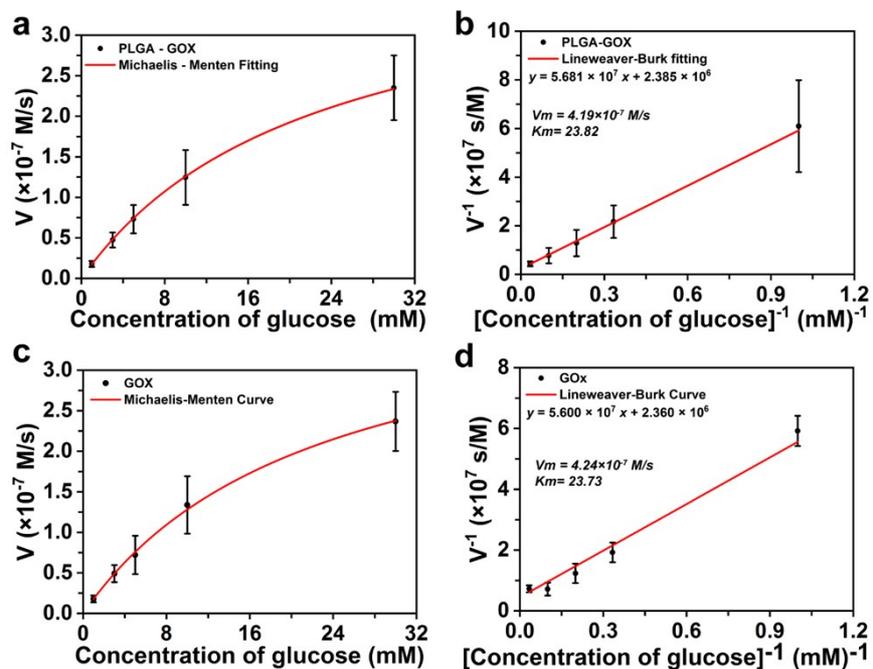


**Fig. S6** *In vitro* ROS generation of IR780@PLGA-GOx as assisted by irradiation with an 808 nm laser ( $1.5 \text{ W/cm}^2$ ) for increasing durations. The concentration of IR780@PLGA-GOx was (a) 1 mg/mL (PLGA equivalence), (b) 2 mg/mL (PLGA equivalence), (c) 3 mg/mL (PLGA equivalence), or (d) 4 mg/mL (PLGA equivalence).

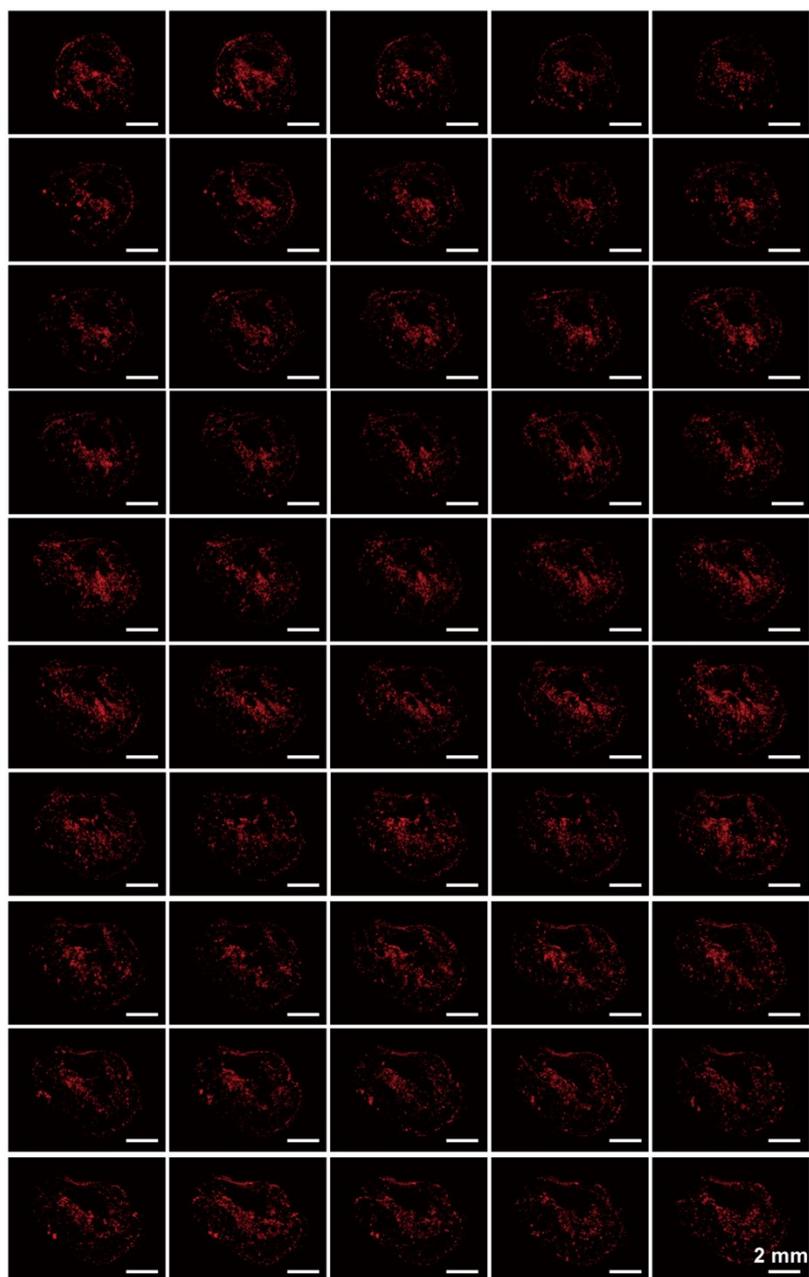


**Fig. S7** *In vitro* ROS generation of different concentrations of IR780@PLGA-GOx as assisted by irradiation with an 808 nm laser ( $1.5 \text{ W/cm}^2$ ). The irradiation time was (a)

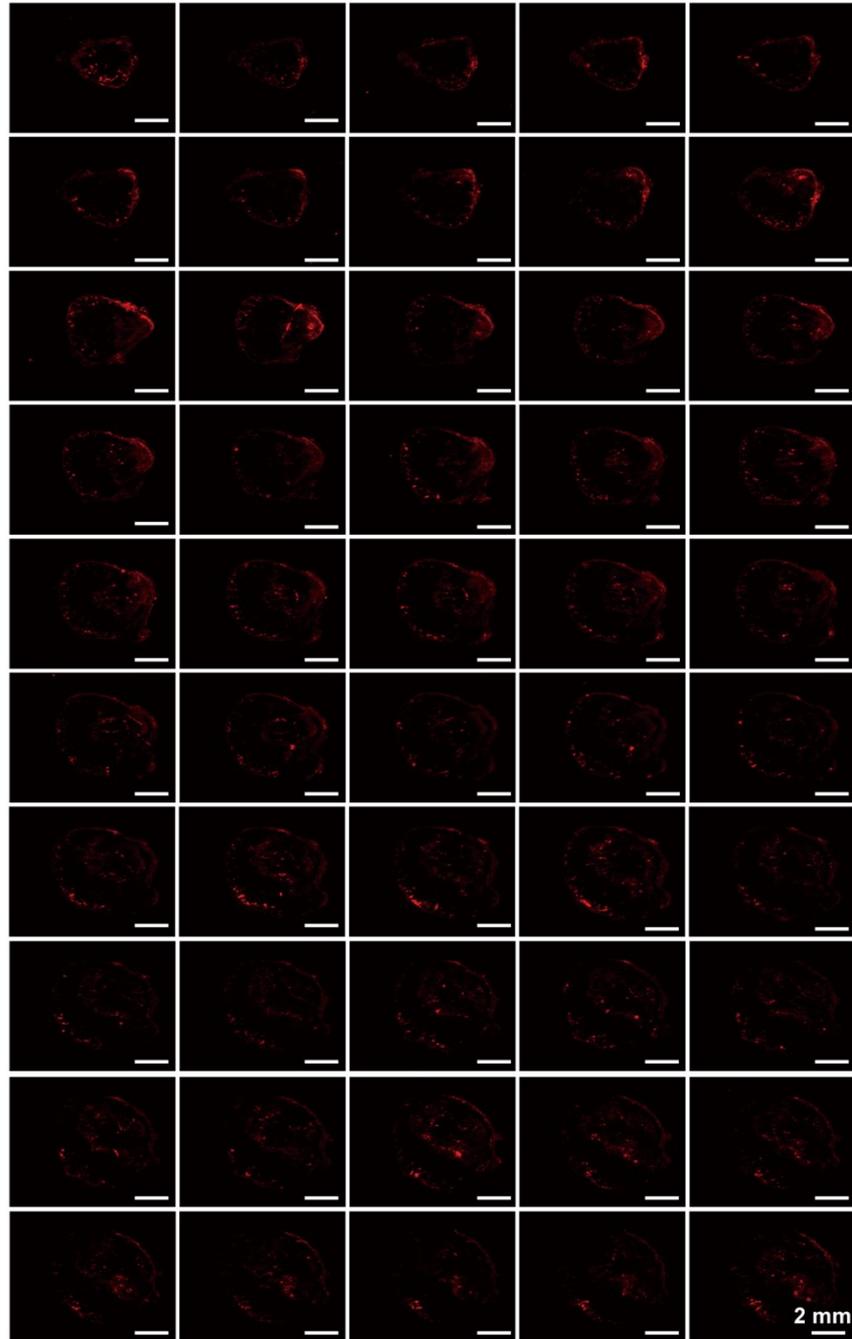
15 s, (b) 30 s, (c) 60 s, or (d) 90 s.



**Fig. S8** (a) Lineweaver–Burk plot of PLGA-GOx; (b) Michaelis–Menten kinetics of PLGA-GOx; (c) Lineweaver–Burk plot of GOx; (d) Michaelis–Menten kinetics of GOx.



**Fig. S9** Tomographic scanning of tumor tissue in 25  $\mu\text{m}$  intervals after intravenous injection of IR780@PLGA-GOx.



**Fig. S10** Tomographic scanning of tumor tissue with 25  $\mu\text{m}$  intervals after intravenous injection of PLGA-GOx.

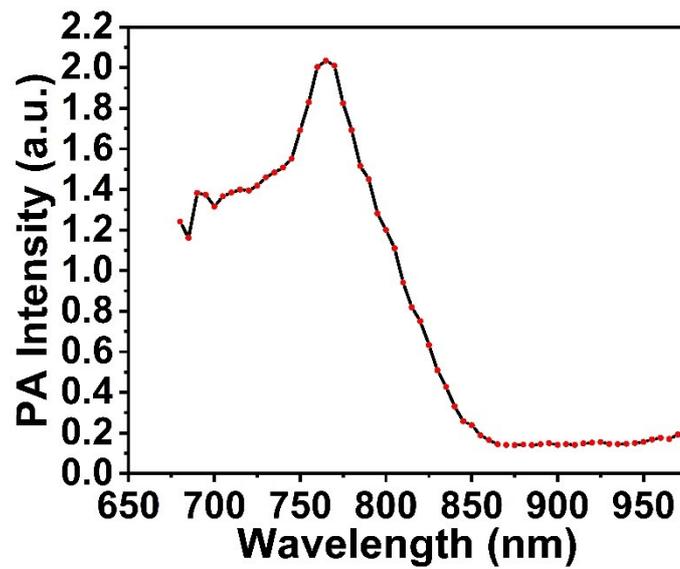


Fig. S11 PA intensity of IR780@PLGA-GOx excitation at wavelengths from 680 to 970 nm.

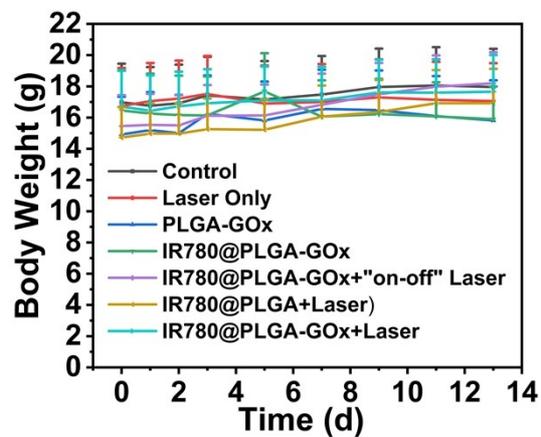
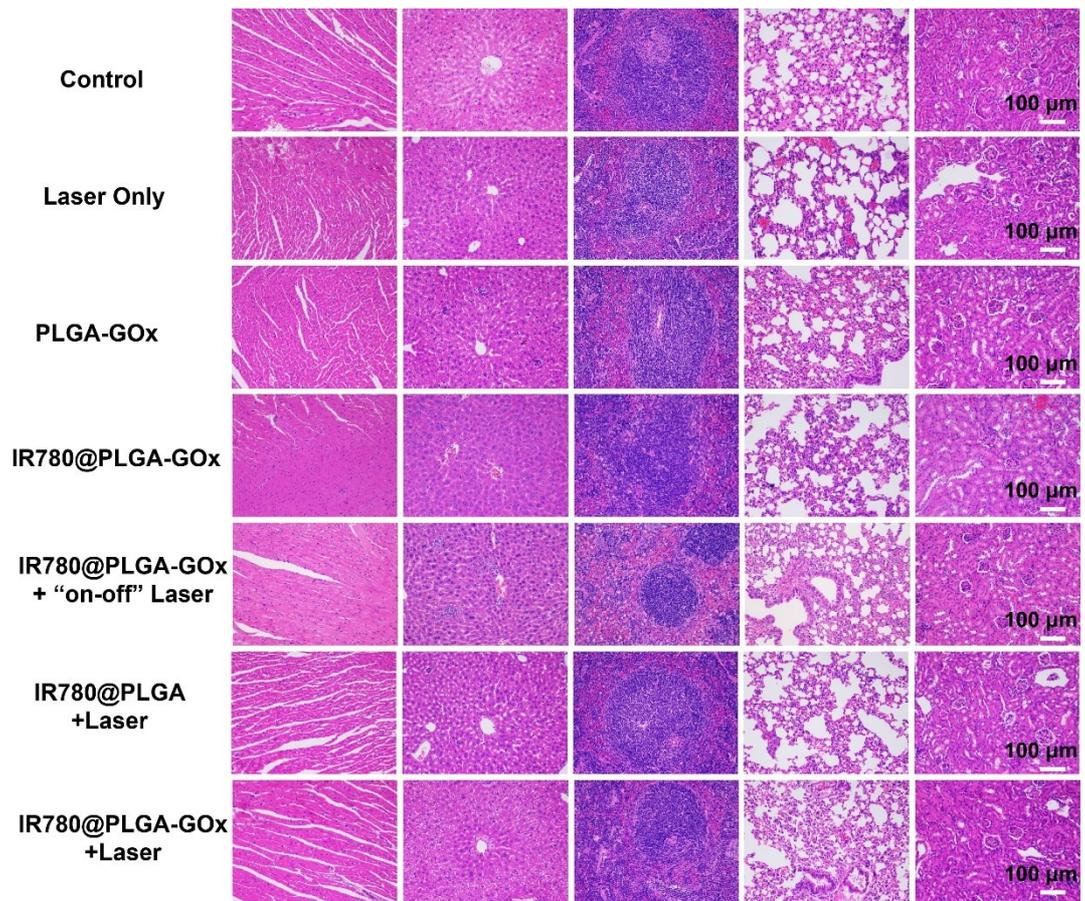


Fig. S12 Body weights of the mice in each group during the treatment period (n = 5).



**Fig. S13** H&E staining of major organs, including the heart, liver, spleen, lungs and kidneys, of 4T1 tumor-bearing mice post treatment (scale bar: 100  $\mu$ m).