Supplementary Information

Temperature-controlled, phase-transition ultrasound imaging-guided photothermal-chemotherapy triggered by NIR light

Wei Li[#1], Wanqing Hou[#1], Xiaomeng Guo[1], Lihua Luo[1], Qingpo Li[1], Chunqi Zhu[1], Jie Yang[1], Jiang Zhu[2], Yongzhong Du[1], Jian You*[1]

[1]College of Pharmaceutical Sciences, Zhejiang University, Yuhangtang Road 866, Hangzhou 310058, People's Republic of China

[2]Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou 310016, People's Republic of China

[#] These authors contributed equally to this work

* Corresponding Author:

Jian You, College of Pharmaceutical Sciences, Zhejiang University, Yuhangtang Road 866, Hangzhou 310058, People's Republic of China; Tel: 086-571-88981651; Fax: 086-571-88208439; E-mail: youjiandoc@zju.edu.cn.

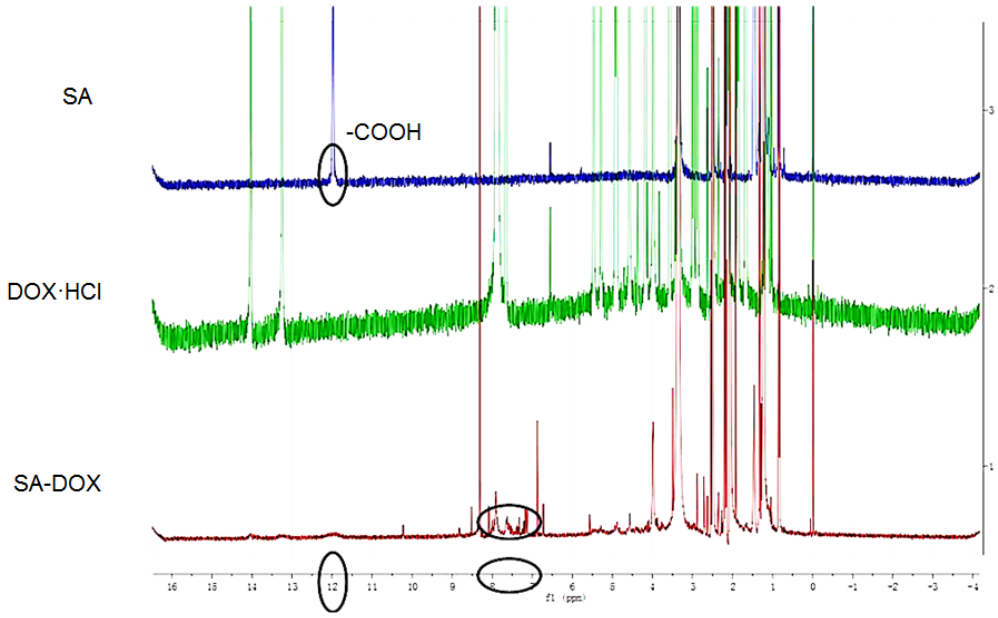

Figure S1. The ^{1}H-NMR spectra of SA, DOX·HCl and SA-DOX.

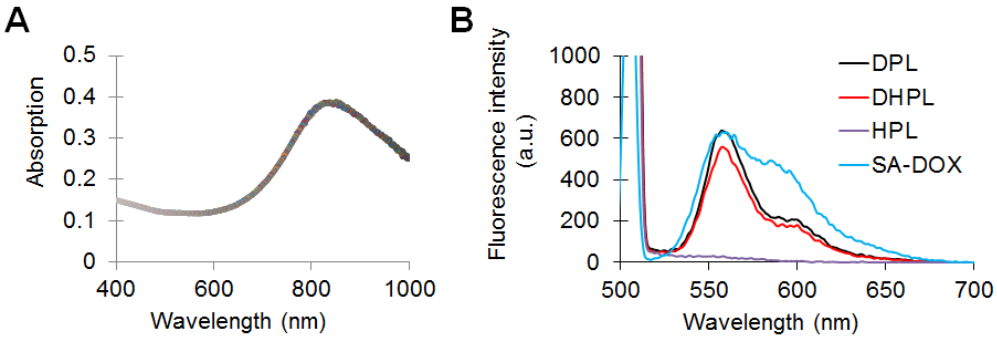

Figure S2. UV-vis and fluorescence spectra. (A) UV-vis absorption spectrum of HAuNS. **(B)** Fluorescence spectra of SA-DOX, DPL, HPL and DHPL (DOX/HAuNS concentration: 2.5 μg/mL).

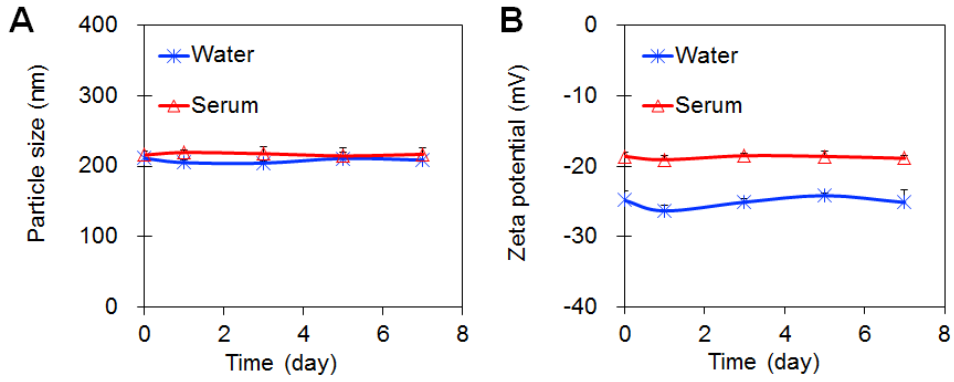

Figure S3. Stability of DHPL. (A) Particle size change of DHPL in one week (n=3). **(B)** Zeta potential change of DHPL in one week (n=3).

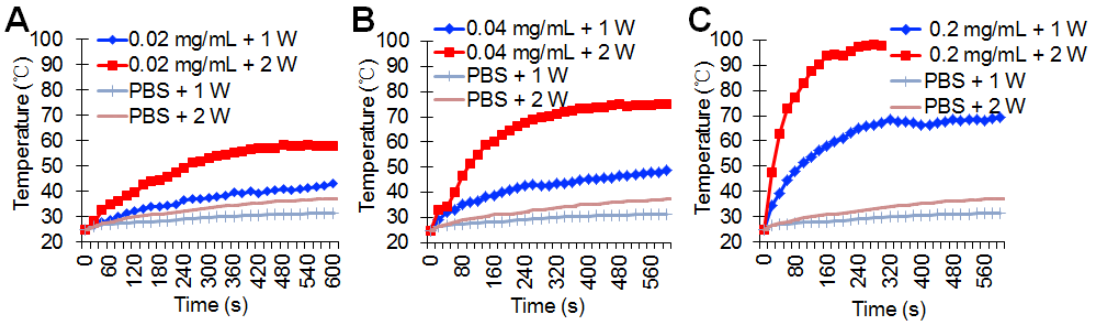

Figure S4. Photothermal effect of DHPL-59 under laser irradiation. (A) Temperature elevation curves of DHPL-59 (HAuNS: 0.02 mg/mL) or PBS under 1 W/cm^2 or 2 W/cm^2 NIR laser. **(B)** Temperature elevation curves of DHPL-59 (HAuNS: 0.04 mg/mL) or PBS under 1 W/cm^2 or 2 W/cm^2 NIR laser. **(C)** Temperature elevation curves of DHPL-59 (HAuNS: 0.2 mg/mL) or PBS under 1 W/cm^2 or 2 W/cm^2 NIR laser.

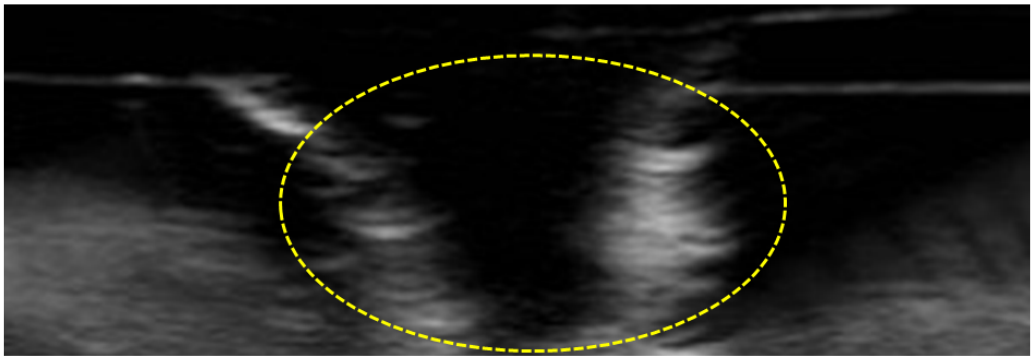

Figure S5. Ultrasound imaging of DHPL solution after "turn-off".

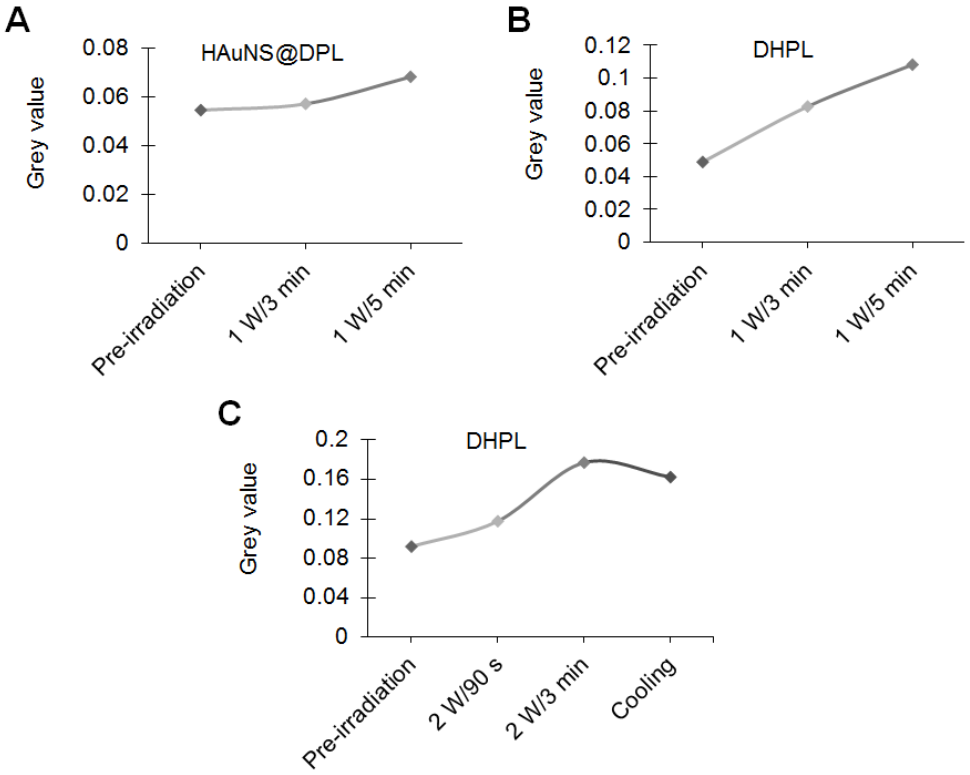

Figure S6. Gray value of the ultrasound signal of HAuNS@DPL **(A)**, DHPL **(B)**, and DHPL (cool down after laser treatment) **(C)** in the region of interest (ROI) under laser irradiation analyzed by "Image J" software.

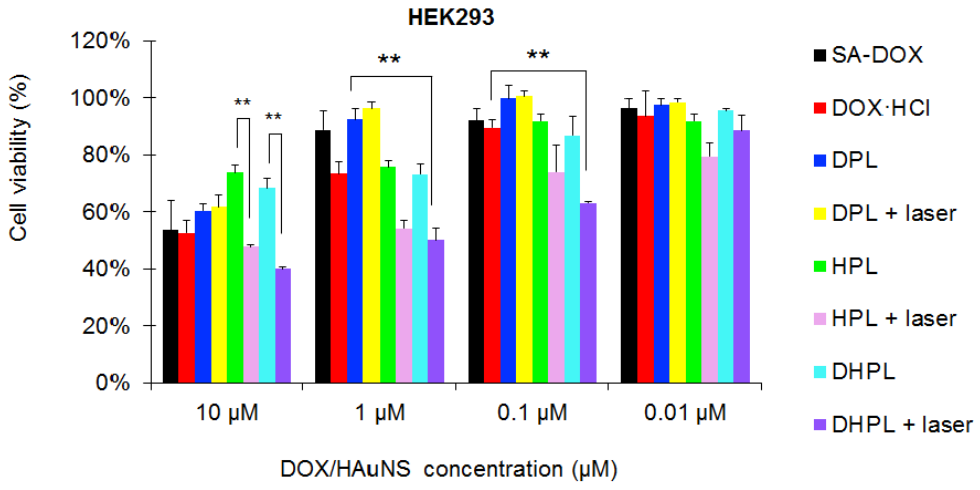

Figure S7. Cytotoxicity to HEK293 cells. Cell viability of HEK293 cells treated with SA-DOX, DOX·HCl, DPL, HPL, and DHPL followed by NIR light irradiation (1 W/cm^2, 3 min). Cells without laser irradiation were used as controls.

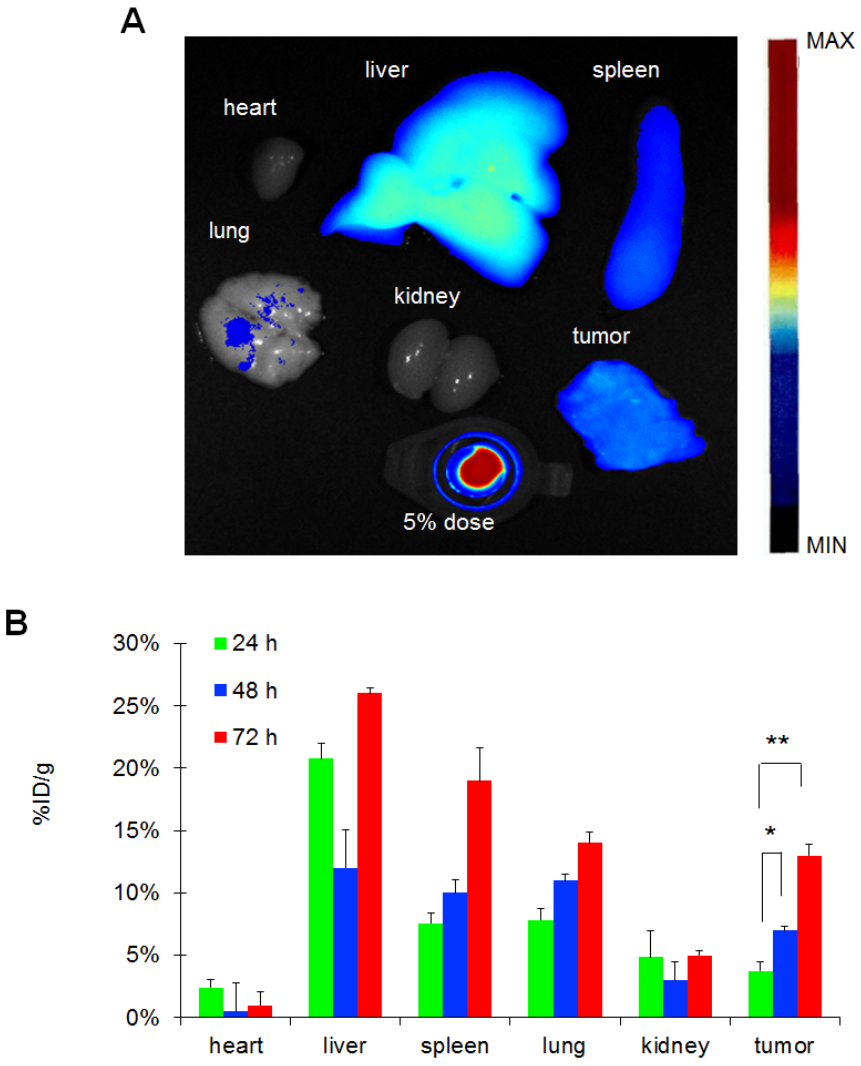

Figure S8. Biodistribution of DHPL. (A) The fluorescence imaging of various tissues at 72 h post-administration. Ex: 748 nm; Em: 780 nm. **(B)** Semi-quantitative fluorescence analysis of DiR-labeled DHPL in heart, liver, spleen, lung, kidney and tumor at 24, 48 or 72 h post-administration (% ID/g).

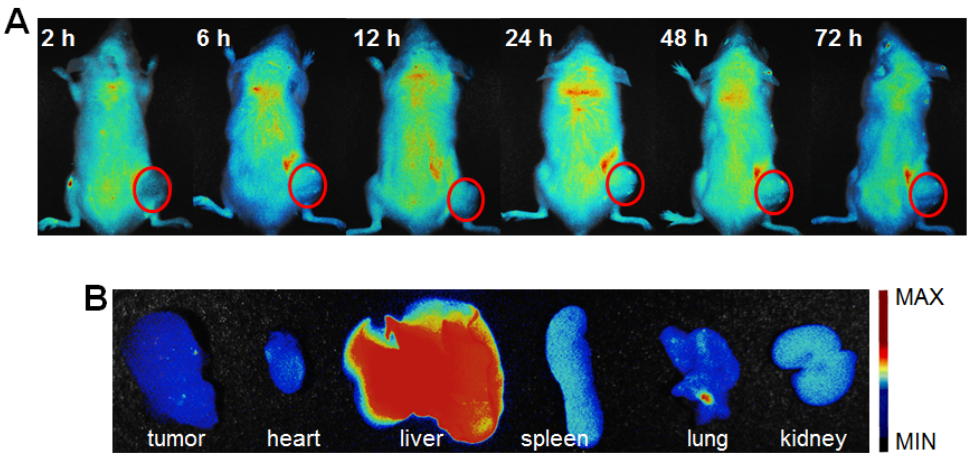

Figure S9. Biodistribution of free DiR. (A) Representative *in vivo* fluorescence imaging of the 4T1 tumor bearing mice at different time point after *i.v.* injection of free DiR. The red circles indicate tumors. Ex: 748 nm; Em: 780 nm. **(B)** The fluorescence imaging of various tissues at 72 h post-administration.

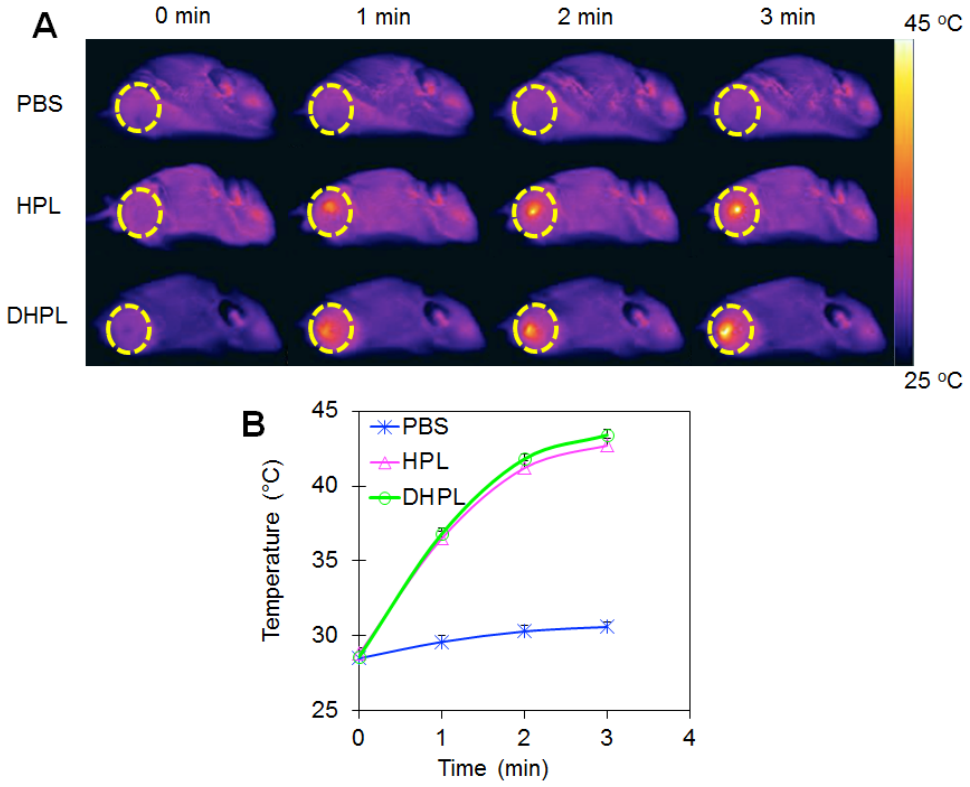

Figure S10. Thermal imaging. (A) Thermal imaging of NIR light-induced temperature elevation at tumor sites 24 h post-injection of HPL or DHPL (5 mg/kg HAuNS). **(B)** The corresponding temperature elevation curves in 3 min.

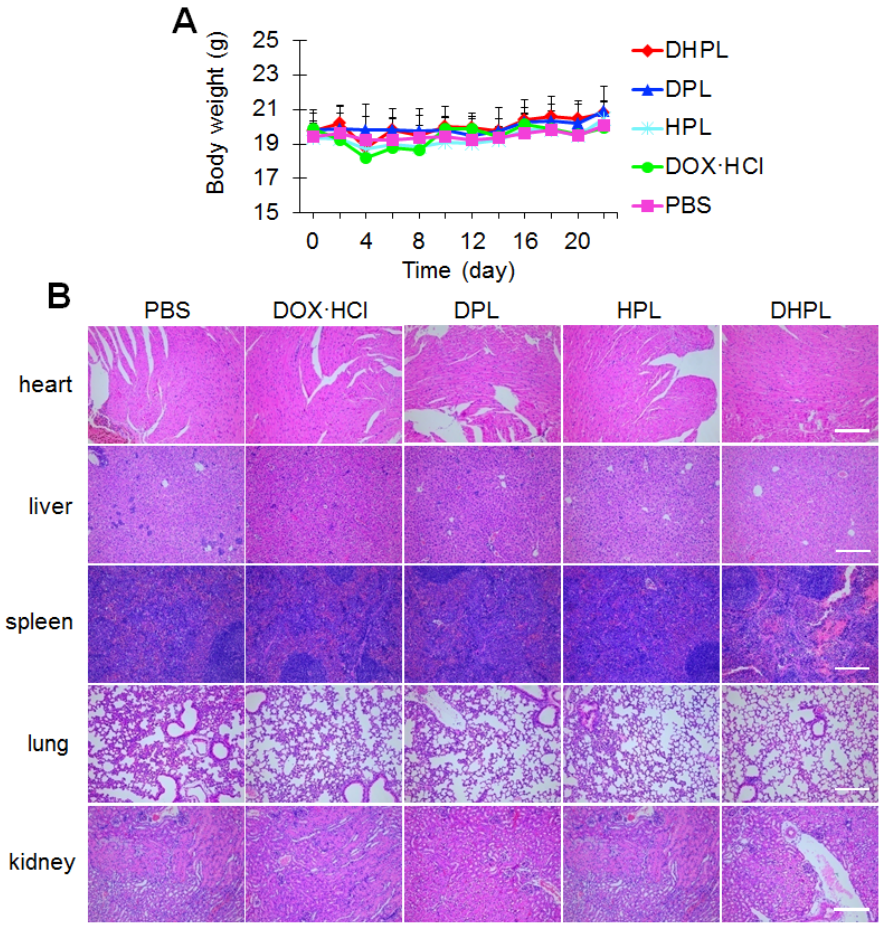

Figure S11. Safety study. (A) The body weight change curves of each group (n=7) in 22 days. **(B)** H&E-stained slices of major tissues. Scale bars, 100 μm.