## **Supporting Information**

## Photothermal-Hypoxia Sequential Activatable Phase-Change Nanoagent for Mitochondria-

## **Targeting Tumor Synergistic Therapy**

Jia Qu,<sup>a</sup> Dengke Teng,<sup>a</sup> Guoqing Sui,<sup>a</sup> Shihui Guan,<sup>a</sup> Yang Wang,<sup>a</sup> Qimeihui Wang,<sup>a</sup> Yuanqiang Lin,<sup>a</sup> Haitao Ran,<sup>b</sup> Zhigang Wang,<sup>b</sup> and Hui Wang\*<sup>a</sup>

a. Department of Ultrasound, China-Japan Union Hospital of Jilin University, Changchun, Jilin

Province 130033, P.R.China. E-mail: wanghuicjuh@sohu.com.

b. Chongqing Key Laboratory of Ultrasound Molecular Imaging, Institute of Ultrasound Imaging,

Second Affiliated Hospital, Chongqing Medical University, Chongqing 400010, P.R.China.



**Figure S1.** UV–vis–NIR absorbance spectra of (a) IR780 and (b) TPZ at different concentrations.

Table S1. Drug	encapsulation	efficiency of	f diffrent n	anoparticles.

	Lauric acid	Stearic acid	Mixture fatty acid
TPZ	35.1%	27.2%	43.3%
IR780	46.1%	39.9%	81.5%



Figure S2. The size changes of PCM@Lip/IT NPs at different temperature for 4h.



**Figure S3.** (a)The size changes of PCM@Lip/IT NPs at 4°C for various days. (b) The size changes of PCM@Lip/IT NPs in PBS, serum and acid PBS.



**Figure S4.** (a) ROS production of PCM@Lip/IT NPs irradiated by 808 nm laser (1.0 W/cm<sup>2</sup>) during different time and (b) its linear correlation. The concentration of IR780 was 15  $\mu$ g/mL. (c) ROS generation of PCM@Lip/IT NPs irradiated at different concentration of IR780 by 808 nm (1 W/cm<sup>2</sup>, 300 s) and (d) its linear correlation.



**Figure S5.** (a) 3D Confocal images of PCM@Lip/IT co-located with mitochondrial tracker. (b) Free IR780 and PCM@Lip/IT co-located with mitochondrial tracker with or without irradiation.



**Figure S6.** PA-signal tendency of PCM@Lip/IT (CIR780 =  $100 \mu g/mL$ ) under laser (wavelength range of 680-960 nm).



**Figure S7.** The IR thermal images of control, Laser only, PCM@Lip/IT only, and PCM@Lip/IT+Laser group under 808 nm laser (1.0 W/cm<sup>2</sup>, 10 min).



Figure S8. Blood biochemical analysis of control group and target group after injection of PCM@Lip/IT NPs for 4, 8, 16 and 30 days. (n = 5).