## **Supporting Information**

## Polymer Nanoparticles Overcome Drug Resistance by Dual-Targeting Apoptotic Signaling Pathway in Breast Cancer

Ning Li,<sup>†</sup> Dong Gao,<sup>\*,‡</sup> Chen Li,<sup>§</sup> Baiqi Wang,<sup>§</sup> Boying Li,<sup>†</sup> Benkai Bao,<sup>‡</sup> Manman Wu,<sup>‡</sup>

Mengying Li,<sup>#</sup> Chengfen Xing, \*<sup>†,‡</sup>

<sup>†</sup>School of Materials Science and Engineering, Hebei University of Technology, Tianjin, China

\*Key Laboratory of Hebei Province for Molecular Biophysics, Institute of Biophysics, School of

Science, Hebei University of Technology, Tianjin, China

<sup>#</sup>School of Chemical Engineering and Technology, Hebei University of Technology, Tianjin,

## China

<sup>§</sup>Department of Occupational Health and Environmental Health, School of Public Health, Tianjin

Key Laboratory of Environment, Nutrition and Public Health, Tianjin Medical University,

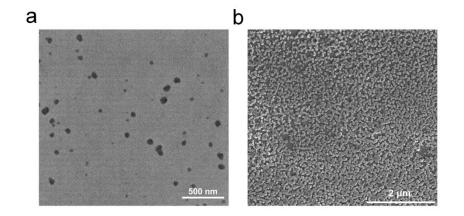
Tianjin, P. R. China, 300070

\* Corresponding Author: Dong Gao, Chengfen Xing

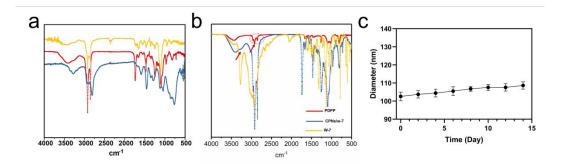
Email: gaodong@iccas.ac.cn, xingc@hebut.edu.cn

KEYWORDS: TRAIL, drug resistance, near-infrared light, dual-targeting, conjugated polymer

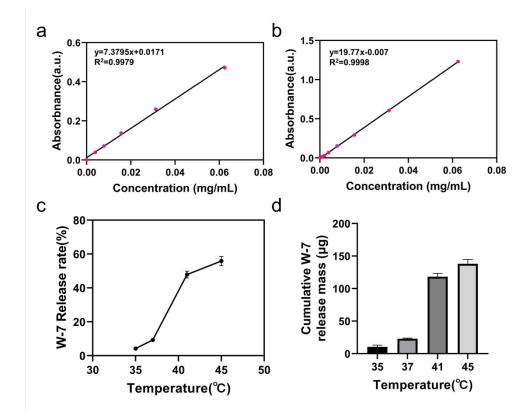
nanoparticles



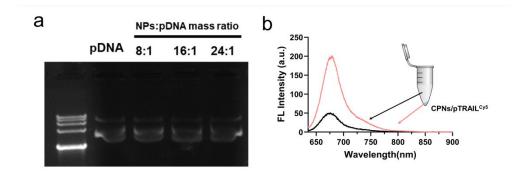
**Figure S1.** (a) TEM images of CPNs (scale bars: 500 nm). (b) SEM images of CPNs (scale bars: 2 μm).



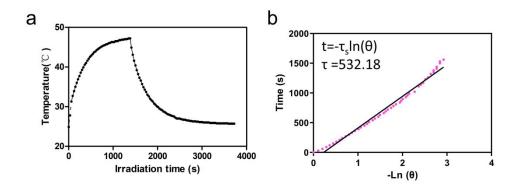
**Figure S2.** (a) FT-IR spectra of DSPE-PEG-PEI, DSPE-PEG-MAL, PEI. Because of PEI modification, the peak at 3421 cm<sup>-1</sup> should be attributed to the stretching and bending vibrations of N–H. (b) FT-IR spectra of PDPP, CPNs/W-7, W-7. (c) DLS data of CPNs/W-7 (10.0  $\mu$ g mL<sup>-1</sup>) aqueous solution after storage at 4 °C under dark for 14 days (n = 3).



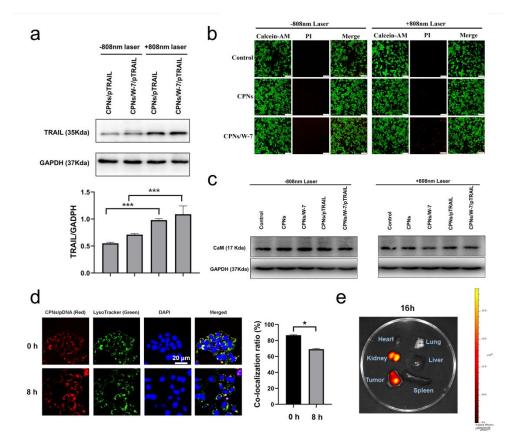
**Figure S3.** (a) Extinction coefficient of PDPP. (b) Extinction coefficient of W-7. (c) Thermally triggered the release of W-7 from CPNs after incubation at different temperature. (d) The cumulative W-7 release mass after incubation at different temperature.



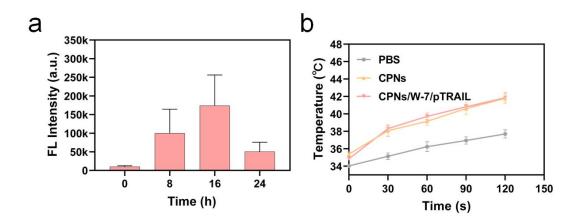
**Figure S4.** (a) Electrophoresis patterns of NPs loaded with pDNA at various mass ratios. The second sample well on the left was for naked pDNA as a control. (b) Fluorescence intensity of CPNs/pTRAILCy5 after density ladder centrifugation.



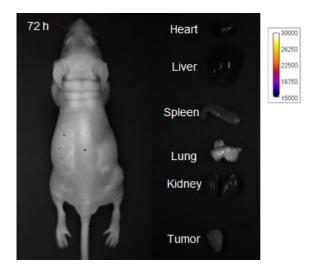
**Figure S5.** Measurement and calculation of photothermal conversion efficiency. (a) Temperature elevation of CPNs (20.0  $\mu$ g mL<sup>-1</sup>) under 808 nm irradiation followed by subsequent cooling to room temperature. (b) Time constant for heat transfer is determined to be  $\tau_s$ = 532.18 s by applying the linear time data from the cooling period versus the negative natural logarithm of driving force temperature, which is obtained from the cooling stage of (a). The photothermal conversion efficiency was calculated to be 55.8% for CPNs.



**Figure S6.** (a) Gene expression of pTRAIL after different treatments as determined by Western blot in 4T1 cells. Undertreatment with CPNs/pTRAIL (10.0  $\mu$ g mL<sup>-1</sup>), CPNs/W-7/pTRAIL (10.0  $\mu$ g mL<sup>-1</sup>) without or with 808 nm laser irradiation for 3 min (1 W cm<sup>-2</sup>), respectively (n = 3, \*\*\*P < 0.001 compared to without 808 nm laser irradiation group). (b) Fluorescence images of MCF-7 cells after different treatment and co-staining results with Calcein-AM (Live, green) and PI (Dead, red). Scale bars: 250  $\mu$ m. (c) MCF-7 cells after the different treatments. The expression of CaM was determined by western blot. (d) Fluorescence confocal microscopy images of cells for investigation endosome escape. Cy5-labeled CPNs/pDNA was stained red, and lysosomes were stained with LysoTracker (Green). (e) Fluorescence imaging of major organs in 4T1 tumorbearing nude mice 16 hours after intravenous administration of CPNs (Cy5).



**Figure S7.** (a) Quantification fluorescence intensity of tumor sites at diverse injection time points (0 h, 8 h, 16 h, 24 h) after tail vein administration of CPNs (Cy5) (Data are presented as mean  $\pm$  SD, n = 3). (b) Corresponding temperature changes at the tumor sites during laser irradiation at 808 nm (1 W cm<sup>-2</sup>) after tail vein administration of PBS, CPNs, and CPNs/W-7/pTRAIL at a post-injection time of 16 h (Data are presented as mean  $\pm$  SD, n = 5).



**Figure S8.** Fluorescence imaging of 4T1 tumor-bearing nude mice and the main organs intravenously administrated with CPNs (Cy5) at 72 h.