

## Supplementary information

### Near-infrared light excited photodynamic anticancer therapy based on UCNP@AIEgen nanocomposite

Shihui Ding,<sup>‡a</sup> Wenbo Wu,<sup>‡b,f</sup> Tingting Peng,<sup>‡c</sup> Wen Pang,<sup>a</sup> Pengfei Jiang,<sup>a</sup> Qiuqiang Zhan,<sup>c</sup> Shuhong Qi,<sup>d,e</sup> Xunbin Wei,<sup>\*a,g,h</sup> Bobo Gu,<sup>\*a</sup> Bin Liu,<sup>\*b</sup>

<sup>a</sup> School of Biomedical Engineering, Shanghai Jiao Tong University, 1954 Huashan Road, Shanghai 200030, China.

<sup>b</sup> Department of Chemical and Biomolecular Engineering, National University of Singapore, 117585, Singapore.

<sup>c</sup> Centre for Optical and Electromagnetic Research, South China Academy of Advanced Optoelectronics, South China Normal University, Guangzhou 510006 China.

<sup>d</sup> Britton Chance Center for Biomedical Photonics, Wuhan National Laboratory for Optoelectronics-Huazhong University of Science and Technology, Wuhan, Hubei 430074, China.

<sup>e</sup> MoE Key Laboratory for Biomedical Photonics, Collaborative Innovation Center for Biomedical Engineering, School of Engineering Sciences, Huazhong University of Science and Technology, Wuhan, Hubei 430074, China

<sup>f</sup> Institute of Molecular Aggregation Science, Tianjin University, Tianjin 300072, China

<sup>g</sup> Biomedical Engineering Department, Peking University, Beijing 100081, China

<sup>h</sup> Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Peking University Cancer Hospital & Institute, Beijing, 100142, China

\*Correspondence should be addressed to X. Wei (xwei@bjmu.edu.cn), B. Gu (bobogu@sjtu.edu.cn), and B. Liu (cheliub@nus.edu.sg)

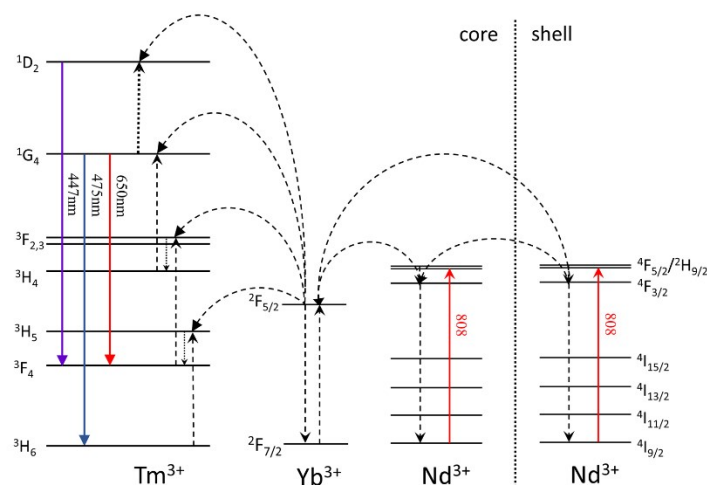


Figure S1. Simplified energy level transition diagram of the synthesized UCNP under 808 nm excitation.

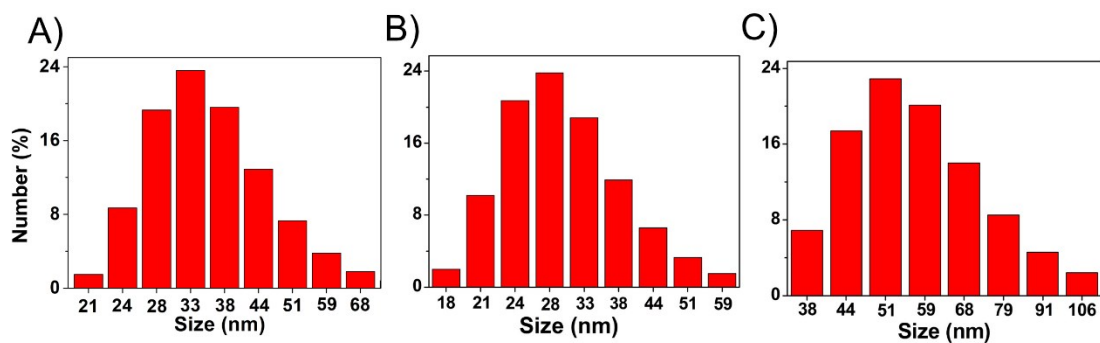


Figure S2. Size distribution of (A) UCNP, (B) TBD dots and (C) UCNP@TBD nanocomposite measured by dynamic light scattering (DLS).

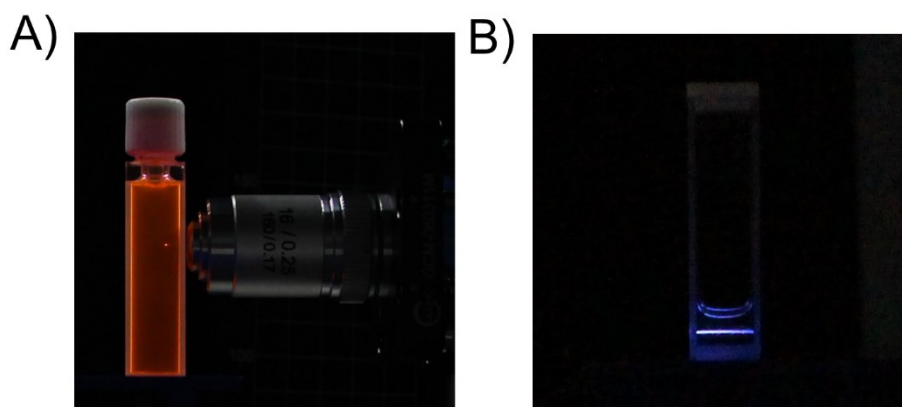


Figure S3. Excitation volume comparison of (A) two-photon excitation (Rhodamine 6G, Ex: 800 nm, 50 mW) and (B) upconversion process (NaYF<sub>4</sub>:30%Yb<sup>3+</sup>, 1%Tm<sup>3+</sup>, 1%Nd<sup>3+</sup> @ NaYF<sub>4</sub>:20%Nd<sup>3+</sup>, Ex: 808 nm, 1W).

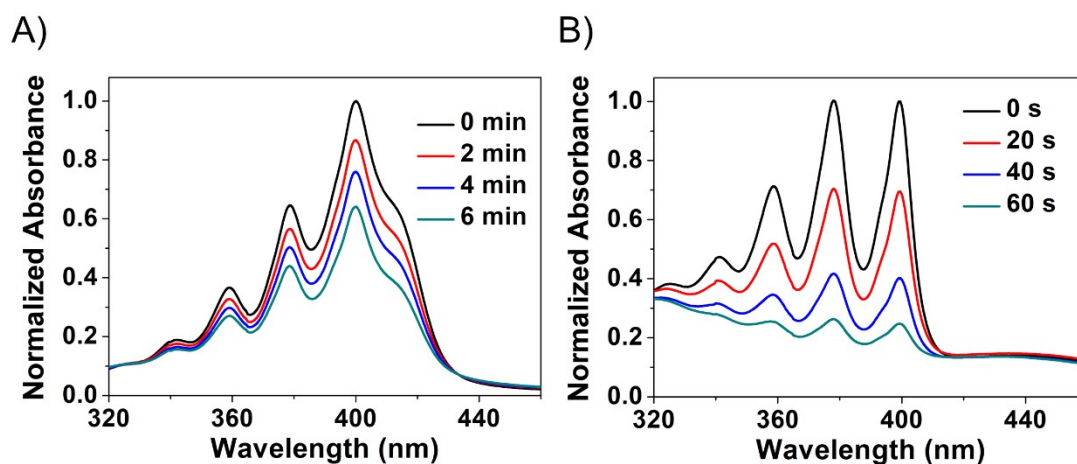


Figure S4. UV-Vis spectra variation of ABDA mixed with (A) Chlorin e6 and (B) TBD dots under white light irradiation (400 - 700 nm, 100 mW/cm<sup>2</sup>) for different time. [Ce6] = 10  $\mu$ M, [TBD dots] = 10  $\mu$ M based on TBD, [ABDA] = 50  $\mu$ M.

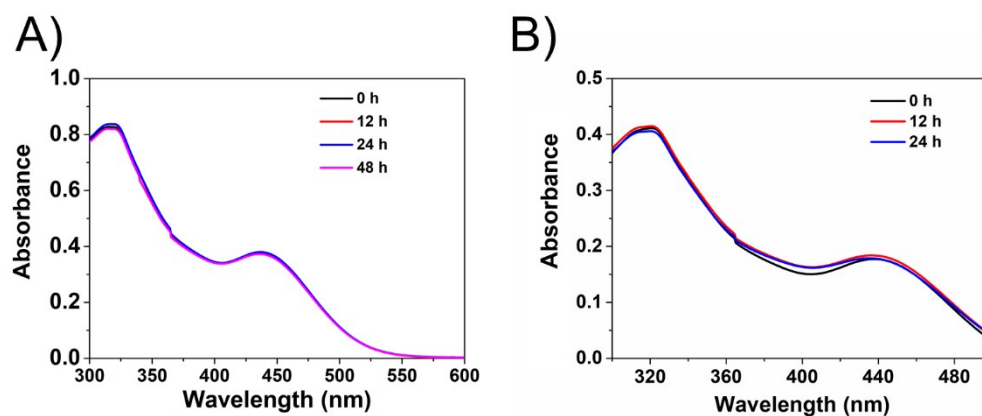


Figure S5. Long-term stability of UCNP@TBD. UV-Vis absorption spectra of UCNP@TBD in (A) aqueous solution and (B) cell lysate at different time. [UCNP@TBD] = 13  $\mu\text{g}/\text{mL}$  based on TBD;  $10^5$  cells were lysed by ultrasonic to form cells lysate.

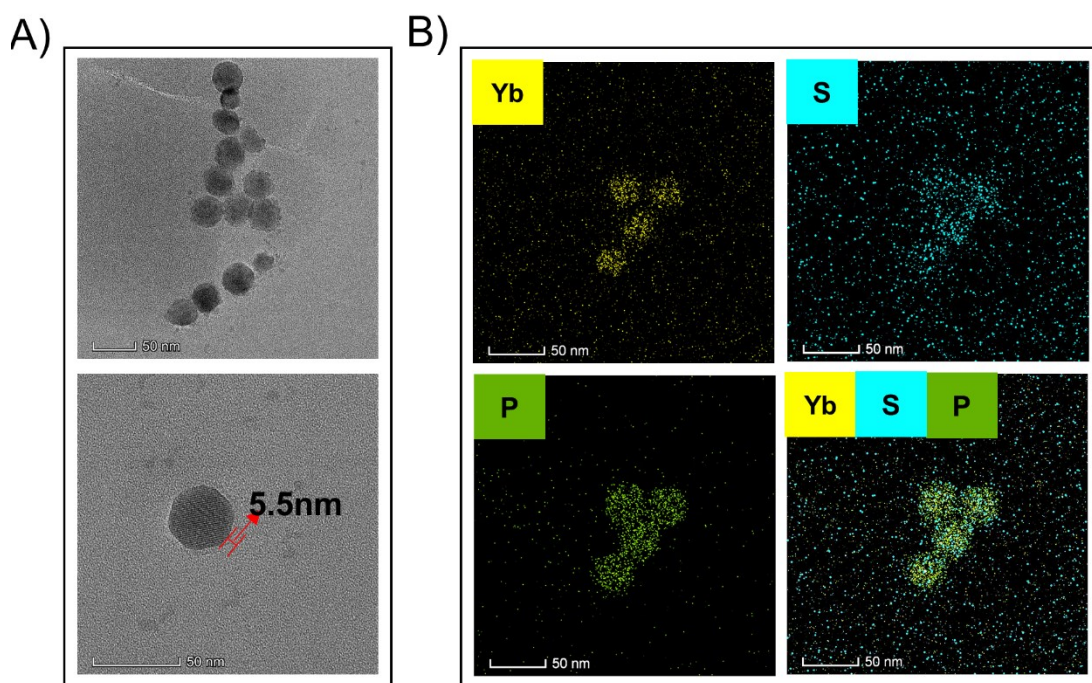


Figure S6. (A) Transmission electron microscopy (TEM) images of UCNP@TBD nanocomposite. (B) Energy-dispersive spectrum (EDS) analysis of ytterbium (Yb), sulfur (S) and phosphorus (P) in UCNP@TBD nanocomposite, which are the characteristic elements of UCNP, TBD and DSPE-PEG-MAL, respectively. Scale bar: 50 nm.

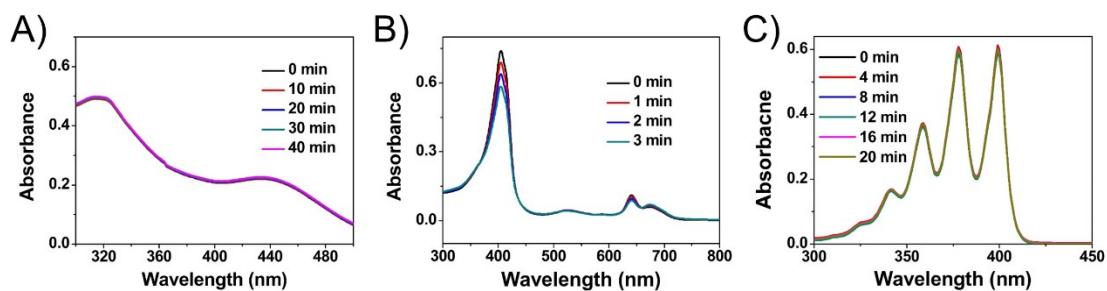


Figure S7. The photostability of different materials. The time-sequenced absorption spectra of (A) UCNP@TBD nanocomposite ([UCNP@TBD] = 15  $\mu\text{g}/\text{mL}$  based on TBD) under the NIR light irradiation (808 nm, 2.5  $\text{W}/\text{cm}^2$ ), (B) Ce6 (10  $\mu\text{M}$ ) under the irradiation (400 - 700 nm,  $\sim 60 \text{ mW}/\text{cm}^2$ ), (C) ABDA (50  $\mu\text{M}$ ) under the NIR light irradiation (808 nm, 200  $\text{mW}/\text{cm}^2$ ) for different time.

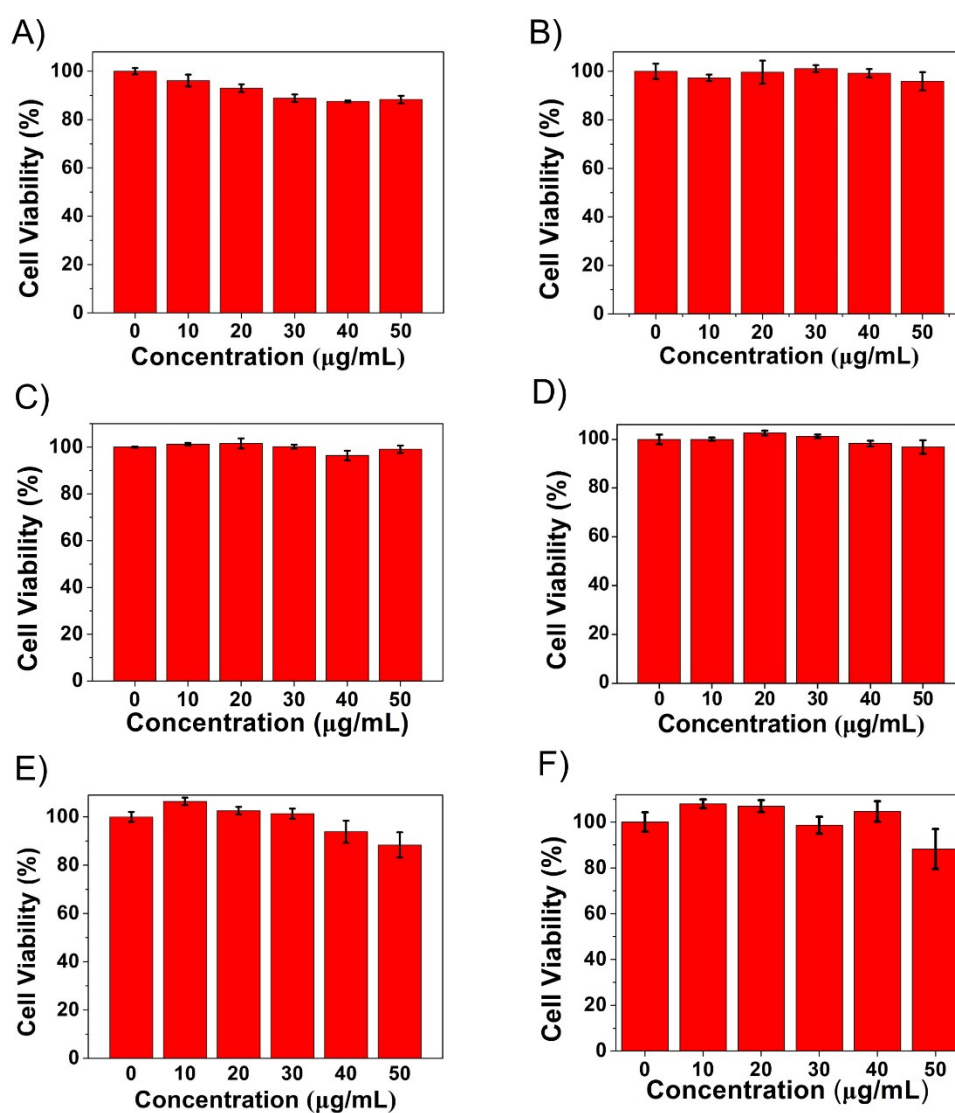


Figure S8. Assessment of biocompatibility of UCNP@TBD and cRGD-UCNP@TBD nanocomposite. Cell viability of 4T1 cells incubated with different concentrations of UCNP@TBD nanocomposite for (A) 24 h and (B) 48 h, and cell viability of HeLa cells were incubated with different concentrations of UCNP@TBD nanocomposite for (C) 24 h and (D) 48 h and cRGD-UCNP@TBD nanocomposite for (e) 24 h and (f) 48 h.

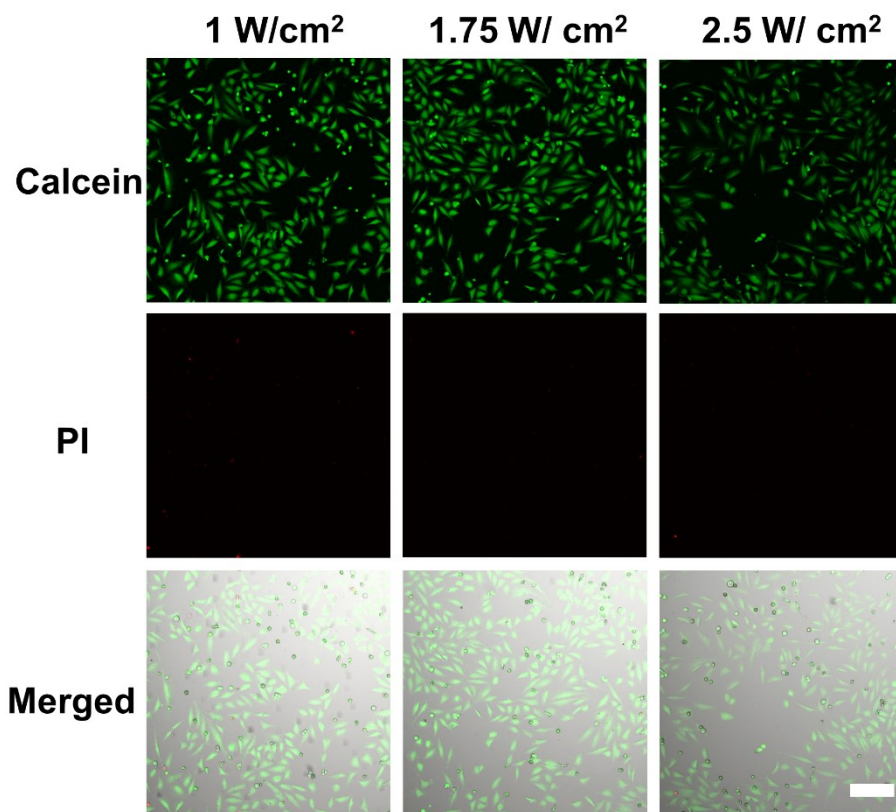


Figure S9. Viability of HeLa cells treated with NIR light irradiation of different power density (808 nm, 1 W/cm<sup>2</sup>, 1.75 W/cm<sup>2</sup>, 2.5 W/cm<sup>2</sup>) for 40 min. Scale bar: 200  $\mu$ m.

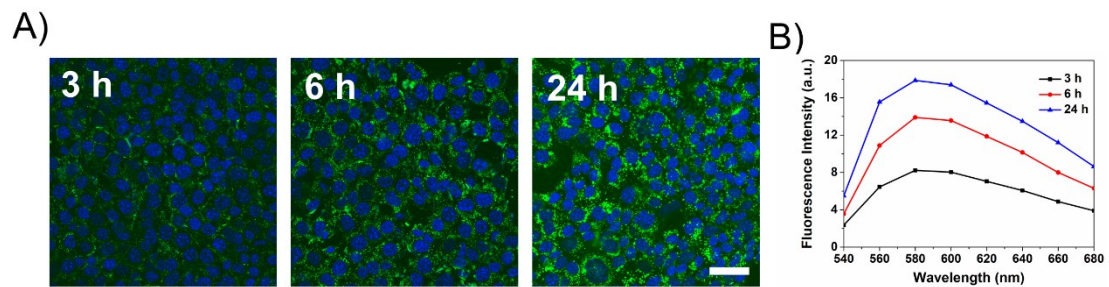


Figure S10. (A) Fluorescence imaging and (B) corresponding spectra of 4T1 cells incubated with both UCNP@TBD nanocomposite ([UCNP@TBD] = 50  $\mu$ g/mL based on TBD) for 3h, 6 h and 24 h and DAPI (1  $\mu$ g/mL) for 15 min, respectively. DAPI (Ex: 405 nm; Em: 420-500 nm), UCNP@TBD (Ex: 488 nm; Em: 555-625 nm). Scale bar: 200  $\mu$ m.

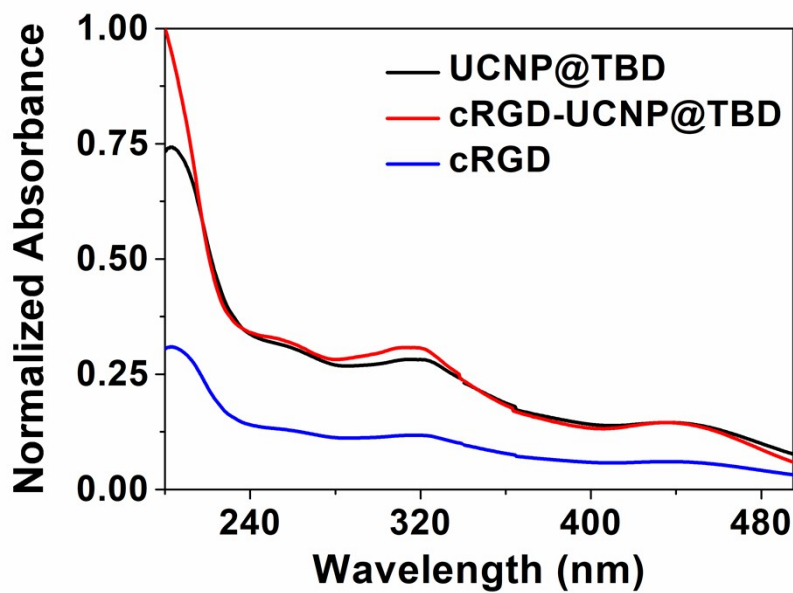


Figure S11. UV-Vis absorption spectra of UCNP@TBD ([UCNP@TBD] = 13  $\mu\text{g}/\text{mL}$  based on TBD), cRGD-UCNP@TBD ([cRGD-UCNP@TBD] = 13  $\mu\text{g}/\text{mL}$  based on TBD) and cRGD (0.2 mg/mL).

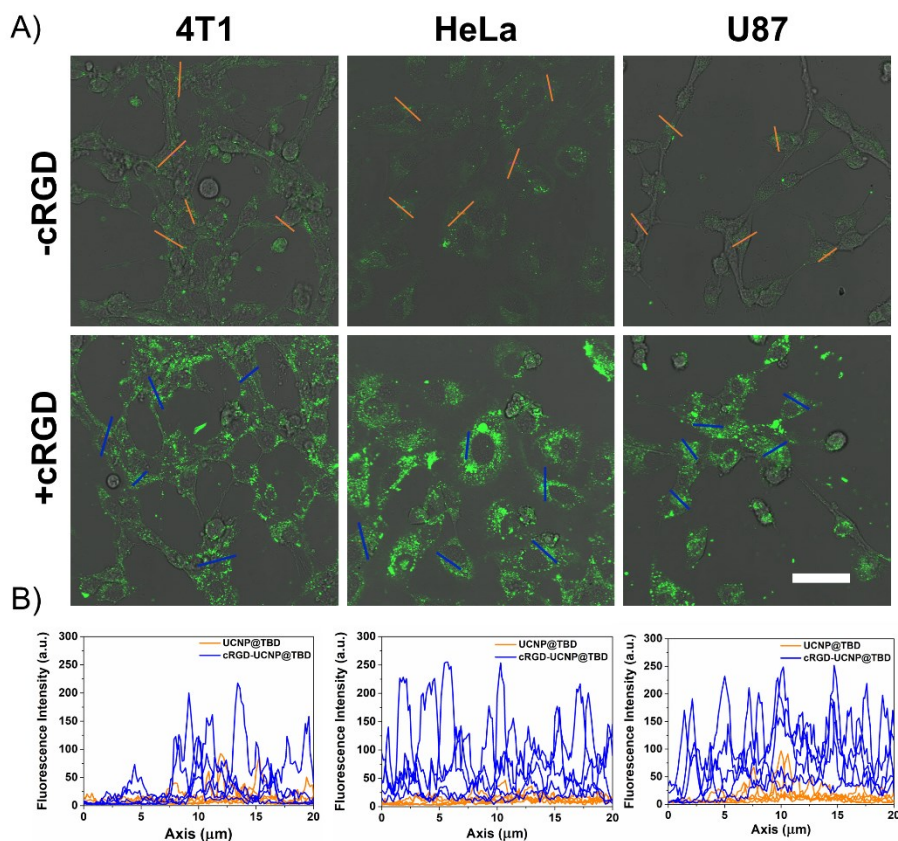


Figure S12. (A) Fluorescence images of and (B) fluorescence intensity line distributions of the marked lines ( $n = 5$ ) in 4T1, U87 and HeLa cells incubated with UCNP@TBD and cRGD-UCNP@TBD nanocomposites ([nanocomposites] = 50  $\mu\text{g}/\text{mL}$  based on TBD) for 6 h. Fluorescence imaging (Ex: 488 nm; Em: 555-625 nm). Scale bar: 200  $\mu\text{m}$ .

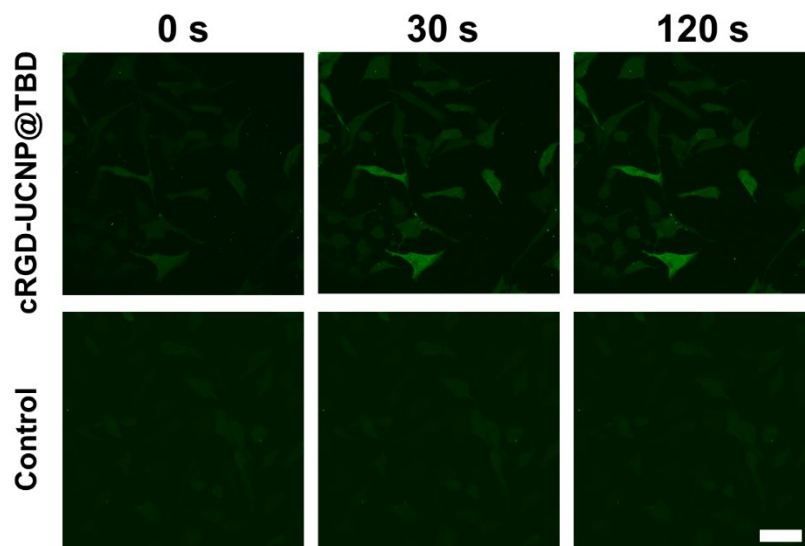


Figure S13. The intracellular ROS generation capability of UCNP@TBD nanocomposite under light irradiation (Ex: 808 nm, 2.5 W/cm<sup>2</sup>). [nanocomposite] = 50 µg/mL based on TBD. DCF (Ex: 488 nm; Em: 500-550 nm). [DCFH-DA] = 5 µM. Scale bar: 200 µm.

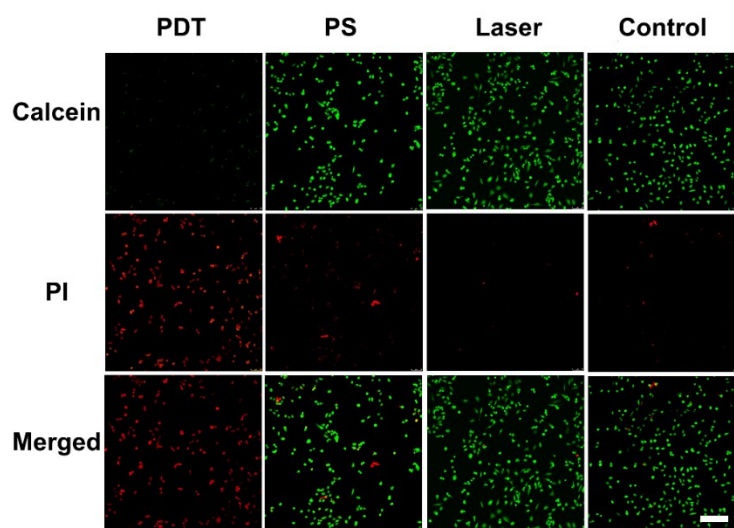


Figure S14. Viability of HeLa cells treated with/without cRGD-UCNP@TBD nanocomposite followed by light irradiation for 40 min (808 nm; 2.5 W/cm<sup>2</sup>) or only treated with cRGD-UCNP@TBD nanocomposite. [cRGD-UCNP@TBD] = 50 µg/mL based on TBD, [Calcein-AM] = 2 µM, [PI] = 2 µM. Calcein-AM (Ex: 488 nm; Em: 505-525 nm) and propidium iodide (PI) (Ex: 552 nm; Em: 605-625 nm). Scale bar: 200 µm.

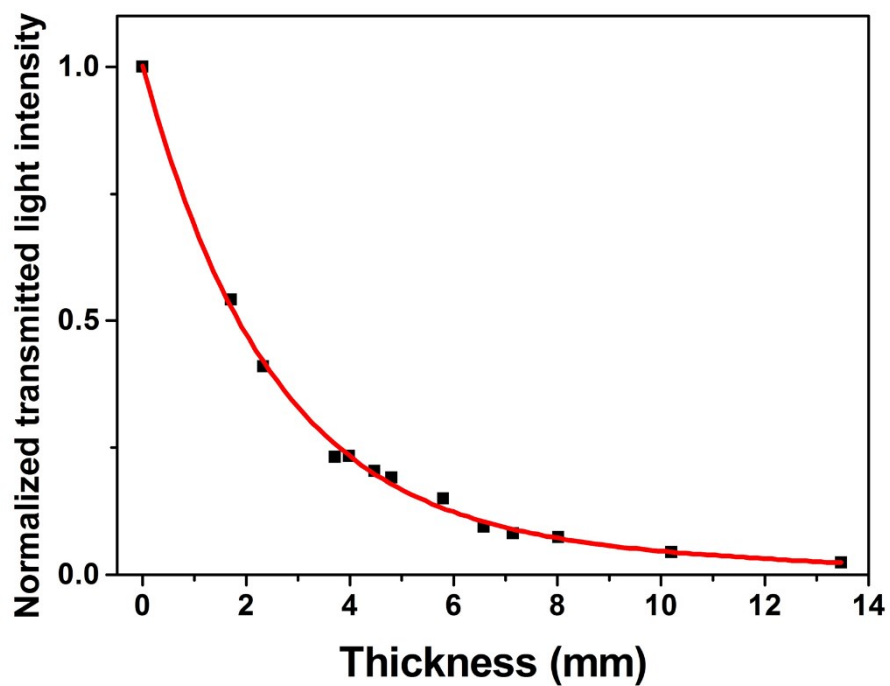


Figure S15. The normalized transmitted NIR light (808 nm) intensity at different thickness of chicken tissues.

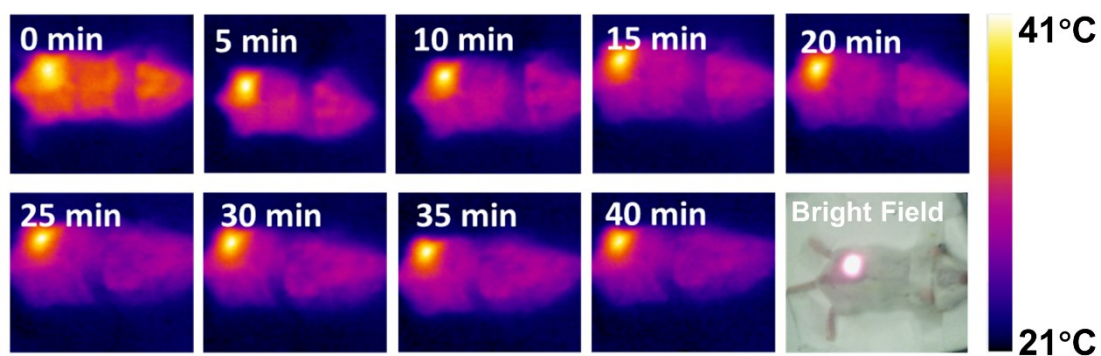


Figure S16. Temperature distribution of tumor-bearing mice treated with UCNP@TBD nanocomposite (10 mg/kg) and continuous laser irradiation (808 nm, 2.5 W/cm<sup>2</sup>). Max temperature: 40.4°C, min temperature: 21.7 °C.