Electronic Supplementary Information (ESI)

Light-activatable Chlorin e6 (Ce6)-imbedded Erythrocyte Membrane Vesicles Camouflaged Prussian Blue Nanoparticles for Synergistic Photothermal and Photodynamic Therapies of Cancer

Lihong Sun^{a, b}, Qian Li^{a, b}, Mengmeng Hou^{a, b}, Ya Gao^{a, b}, Ruihao Yang^{a, b}, Lei Zhang^c, Zhigang Xu^{a, b}, Yuejun Kang^{*a, b}, Peng Xue^{*a, b}

^a Institute for Clean Energy and Advanced Materials, Faculty of Materials and Energy, Southwest University, Chongqing 400715, China. E-mails: <u>xuepeng@swu.edu.cn</u> (P. Xue); <u>yjkang@swu.edu.cn</u> (Y. Kang)

^b Chongqing Engineering Research Center for Micro-

Nano Biomedical Materials and Devices, Chongqing 400715, China.

^c State Key Laboratory of Silkworm Genome Biology, Southwest University, Chongqing 400716, China.



Fig. S1 (a) Fitting curve of the NIR absorbance of PB@RBC/Ce6 NPs at 808 nm as the function of concentration in the range from 0 to 100 ppm; (b) images of PB@RBC/Ce6 NPs dispersed in water, 1×PBS and DMEM culture medium.



Fig. S2 Temperature variation of PB@RBC/Ce6 NPs after irradiation by NIR laser versus the agent concentrations in the range from 0 to 100 ppm.



Fig. S3 Fluorescence microscopic images of RBC, RBC/Ce6 and RBC/Ce6 after hemolysis

(scale bars: 20 μ m).



Fig. S4 (a) Images of Ce6-imbedded RBCs before and after laser irradiation (660 nm, 0.76 W) for 5 min; the red color after RBC disintegration denoted the released hemoglobin; (b) Hemocompatibility tests by incubating RBCs in the solutions of PB@RBC/Ce6 NPs under various concentrations. RBC suspensions in DI water (+) and 1×PBS (–) were also tested as controls.



Fig. S5 CLSM characterization: images of HeLa cells treated with free Ce6 for 0.5 h or 2 h under various magnifications (images of 2^{nd} and 4^{th} row are the enlarged section of dashed box in 1^{st} and 3^{rd} row, respectively). The fluorescence of DAPI and Ce6 are colored as blue and red, respectively (scale bars: 20 µm).



Fig. S6 CLSM characterization: images of HeLa cells treated with PB@RBC/Ce6 NPs for 0.5 h or 2 h under various magnifications (images of 2nd and 4th row are the enlarged section of dashed box in 1st and 3rd row, respectively). The fluorescence of DAPI and Ce6 are colored as blue and red, respectively (scale bars: 20 μm).



Fig. S7 Flow cytometry analysis of the cellular uptake efficiency of Ce6 in 4T1 cells after treatment with (a) PB@RBC/Ce6 NPs or (b) free Ce6 for 0.5 h, 1 h, 2 h, 4 h and 6 h.



Fig. S8 Fluorescence images to exhibit the viability of HUVECs or L929 cells through LIVE/DEAD viability/cytotoxicity assay kit after cells being treated with different concentrations of PB@RBC/Ce6 NPs for 24h. Viable cells were stained with green fluorescence while dead cells were stained with red fluorescence. (Scale bar: $100 \mu m$)



Fig. S9 Primary indicators of blood routine test after healthy mice were intravenously injected with PB@RBC/Ce6 NPs. Reference ranges of hematology data of healthy female KM mice (yellow hatched area) were obtained from Chongqing Tengxin Biotechnology Co. LTD.



Fig. S10 Change of TNF- α level in peripheral blood after KM mice were injected with PB@RBC/Ce6 NPs (equivalent PB concentration: 20 mg·kg⁻¹).

| | Control | 1st day | 2nd day | 7th day | Reference |
|--------------------------|---------------------|---------------------|-------------------|---------------------|-----------|
| | | | | | range |
| WBC (10 ⁹ /L) | 4.03 ± 1.01 | 4.45 ± 0.97 | 4.33 ± 0.95 | 4.275 ± 1.29 | 0.8-6.8 |
| Lymph (109/L) | 3.03 ± 0.84 | 3.125 ± 0.61 | 3.05 ± 0.61 | 2.075 ± 0.11 | 0.7-5.7 |
| Mon (10 ⁹ /L) | 0.18 ± 0.04 | 0.125 ± 0.04 | 0.18 ± 0.04 | 0.15 ± 0.09 | 0.0-0.3 |
| Gran (109/L) | 0.83 ± 0.17 | 1.2 ± 0.34 | 1.1 ± 0.3 | 0.7 ± 0.17 | 0.1-1.8 |
| RBC (1012/L) | 7.77 ± 0.68 | 7.53 ± 0.89 | 8.22 ± 0.55 | 7.2525 ± 0.16 | 6.36-9.42 |
| HGB (g/L) | 120.75 ± 9.42 | 119.75 ± 13.25 | 128.5 ± 8.08 | 117 ± 8.86 | 110-143 |
| HCT (%) | 41.15 ± 2.16 | 40.9 ± 3.78 | 44.45 ± 1.74 | 38.65 ± 1.07 | 34.6-44.6 |
| MCV(fL) | 54.03 ± 1.10 | 54.58 ± 1.66 | 54.17 ± 1.68 | 53.35 ± 0.50 | 48.2-58.3 |
| MCH (pg) | 16.25 ± 0.11 | 15.95 ± 0.47 | 15.9 ± 0.32 | 16.35 ± 0.49 | 15,8-19.0 |
| MCHC (g/L) | 308 ± 2.23 | 306.5 ± 13.5 | 313.5 ± 46.40 | 312.75 ± 10.83 | 302-353 |
| RDW (%) | 16.25 ± 0.66 | 143.05 ± 218.79 | 16.3 ± 0.50 | 16.3 ± 0.41 | 13.0-17.0 |
| PLT (10 ⁹ /L) | 718.75 ± 137.52 | 600.25 ± 125.67 | 479.25 ± 9.39 | 875.75 ± 125.91 | 450-1590 |
| MPV(fL) | 5.6 ± 0.21 | 5.48 ± 0.35 | 5.78 ± 0.19 | 5.78 ± 0.11 | 3.8-6.0 |
| PDW | 16.38 ± 0.25 | 16.23 ± 0.40 | 16.75 ± 0.21 | 16.01 ± 0.42 | - |
| PCT (%) | 0.40 ± 0.08 | 0.27 ± 0.10 | 0.15 ± 0.07 | 0.51 ± 0.08 | - |

Table S1 Complete indicators of blood examinations after healthy mice were injected with

PB@RBC/Ce6 NPs.