Supporting Information

Materials and Methods

Cell culture

Human tumor cell lines including MDA-MB-231, MDA-MB-468 were purchased from Institute of Peking Union Medical College, Basic Medical Sciences and Chinese Academy of Medical Sciences (Beijing, China). Both cell lines were cultured in DMEM supplemented with 10% heat-inactivated FBS, penicillin (100 U/mL), and streptomycin (100 U/mL). HBMECs cell line was cultured in endothelial cell medium (ECM) supplemented with 5% FBS, penicillin (100 U/mL), streptomycin (100 U/mL), and 1% endothelial cell growth supplement (ECGS).

Evaluation of CXCR4 expression in tumor cells

To evaluate the expression levels of CXCR4 receptors in 4T1, MCF-7, MDA-MB-231 and MDA-MB-468 tumor cells, western blotting analysis was carried out. Briefly, protein lysates from 4 kinds of cell lines were extracted in RIPA lysis buffer in the presence of phosphatase inhibitors mixture, respectively. Total protein (50 μg for each sample) that quantified by the bicinchononic acid (BCA) assay (Thermo scientific, USA) was separated by the 10% bis-tris gel (Invitrogen, USA), and transferred to a PVDF membrane (0.45 μm, Millipore, USA). Blots were incubated with 5% (w/v) nonfat milk in tris-buffered saline containing 0.1% Tween-20 (TBST) at room temperature for 45 min. After being washed with TBST for three times, the blots were incubated with anti-CXCR4 primary antibody (1: 1000; Abcam, U.K) overnight at 4 °C. Then blots were further incubated with horseradish peroxidase (HRP) conjugated anti-rabbit IgG at 1: 1000 dilution for 2 h at room temperature. After being washed with TBST for three times, the immunocomplex on each bolt was visualized using ChemiDoc® Touch Imaging System (Bio-Rad, USA) after treatment with SuperSignal® West Femto Maximum Sensitivity Substrate (Thermo Scientific, USA).

In vitro drug release behaviors of doxorubicin

The drug release behaviors of doxorubicin *in vitro* were detected based on the dialysis method at 37 °C in PBS buffer (pH 7.4). Briefly, pLipo-DOX-ICG (10 mL) was put in a dialysis bag with molecular weight cut-off of 5 kDa, and then immersed into 50 mL PBS buffer. Samples were irradiated by an 808 nm NIR laser at 1.5 W/cm^2 for 3 min. The same sample of pLipo-DOX-ICG (10 mL) without NIR laser irradiation was used as the control group. For each predesigned time interval, 3 mL of the PBS solution was taken out and tested by the UV-vis spectrophotometer at the wavelength of 570 nm to quantify the amount of released doxorubicin. After that, 3 mL of fresh PBS solution was further introduced to maintain consistence.

Systemic toxicity evaluation

At the endpoint of experiment, tumor-bearing mice were killed by cervical vertebra dislocation. Tumors and major organs (heart, liver, spleen, lung and kidney) were immediately harvested, weighed, and hematoxylinand eosin (H&E) staining. Simultaneously, the serum of tumor-bearing mice were collected for biochemical indicator analysis including alanine aminotransferase (ALT), alkaline phosphatase (ALP), aspartate transaminase (AST), triacylglycerol (TG), creatinine (CRE), blood urea nitrogen (BUN) and blood glucose (GLU), respectively.

Figures and Figure captions

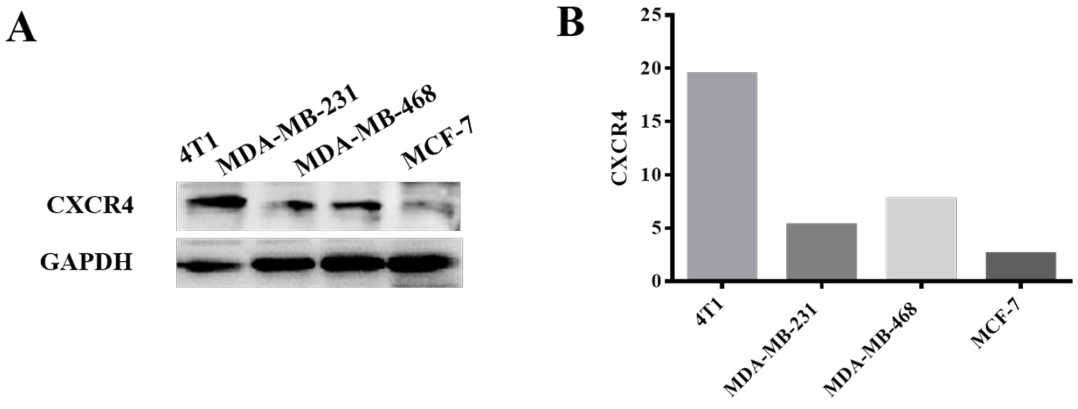

Figure S1. Western blotting analysis and the semi-quantitative analysis of CXCR4 expression levels in 4T1, MDA-MB-231, MDA-MB-468, and MCF-7 cells. GAPDH was used as a normalized control.

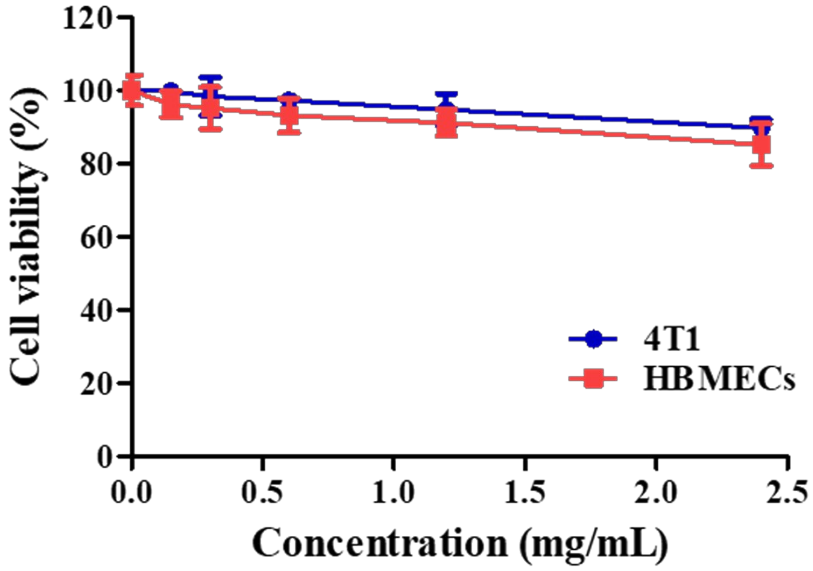

Figure S2. Normal cells line of HBMECs and tumor cell line of 4T1 were incubated with different concentrations of pLipo for 24 h at 37 °C. Then *in vitro* cytotoxicity of pLipo was evaluated by the CCK-8 assay. Cells treated with PBS alone were used as controls. Error bars represent standard deviation (SD), and data are presented as the mean ± SD (*n* = 5).

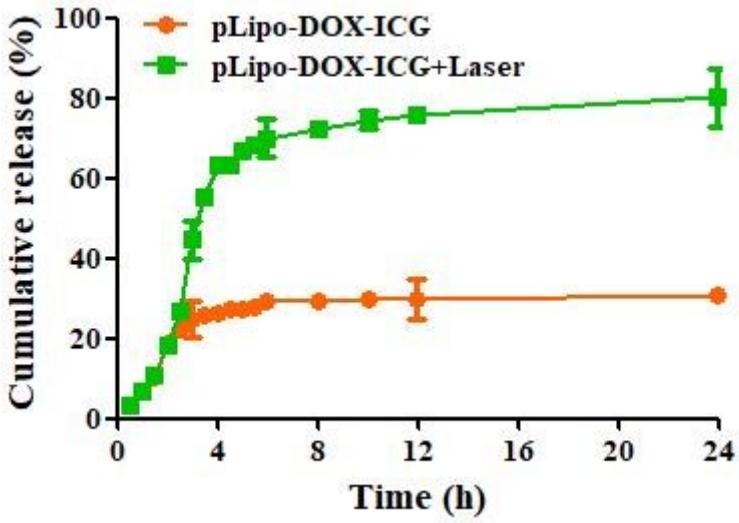

Figure S3: Time course (0-24 h) release profiles of doxorubicin from pLipo-DOX-ICG at 37 °C after NIR laser irradiation at 1.5 W/cm^2 for 3 min (808 nm). The same sample of pLipo-DOX-ICG (10 mL) without NIR laser irradiation was used as the control group. Data are presented as mean ± SD (*n* = 3).

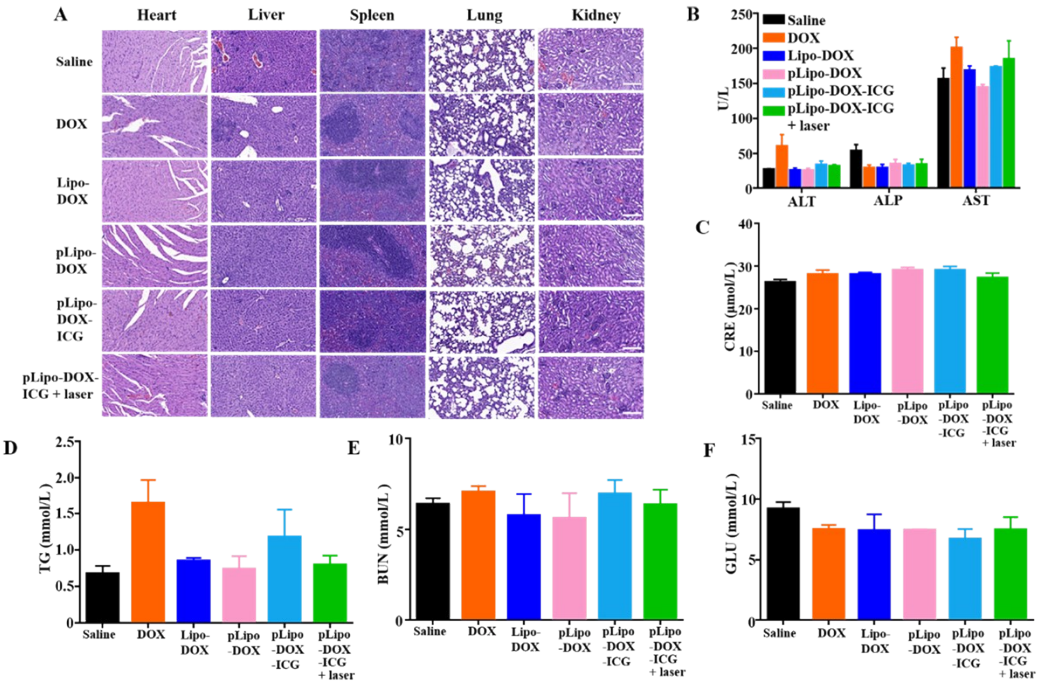

Figure S4. (A) Histological analysis of major organs (heart, liver, spleen, lung, and kidney) derived from mice after treatment with saline, DOX, Lipo-DOX, pLipo-DOX, and pLipo-DOX-ICG with or without NIR laser irradiation, respectively. Scale bar = 100 μm. (B-F) Blood biochemistry analysis of mice after treatment with saline, DOX, Lipo-DOX, pLipo-DOX, and pLipo-DOX-ICG with or without NIR laser irradiation, such as ALT, ALP, AST, CRE, TG, BUN and GLU. Data are presented as the mean ± SD (n = 5).