Supporting information

Title:

NIR-light-trigger delivery of Doxorubicin-loaded PLGA nanoparticles for synergistic cancer therapy on DMBA/TPA induced tumor mice

Authors:

Tunazzina Zaman Khan [a,1], Shekh Md Newaj [a,1], Ashikur Rahman [a], Rahnuma Tabassum [a], Khandaker Nujhat Tasnim [a], Hasan Mahmud Reza [a], Md. Selim Reza [b], Seonki Hong [c], Shazid Md. Sharker [a, *]

Affiliation:

[a] Department of Pharmaceutical Sciences, North South University, Dhaka-1229, Bangladesh. E-mail: shazid.sharker@northsouth.edu

[b] Department of Pharmaceutical Technology, University of Dhaka, Dhaka-1000, Bangladesh.

[c] Department of Physics and Chemistry, Daegu Gyeongbuk Institute of Science and Technology (DGIST), Daegu, Republic of Korea

[1] Contribute equally to this work.

* Corresponding author:
Dr. Shazid Md. Sharker
Associate Professor
Department of Pharmaceutical Sciences
North South University
Dhaka-1229, Bangladesh
Office: +880-2-55668200, Ext: 6402
Fax: 880-2-885-2016
E-mail: shazid.sharker@northsouth.edu

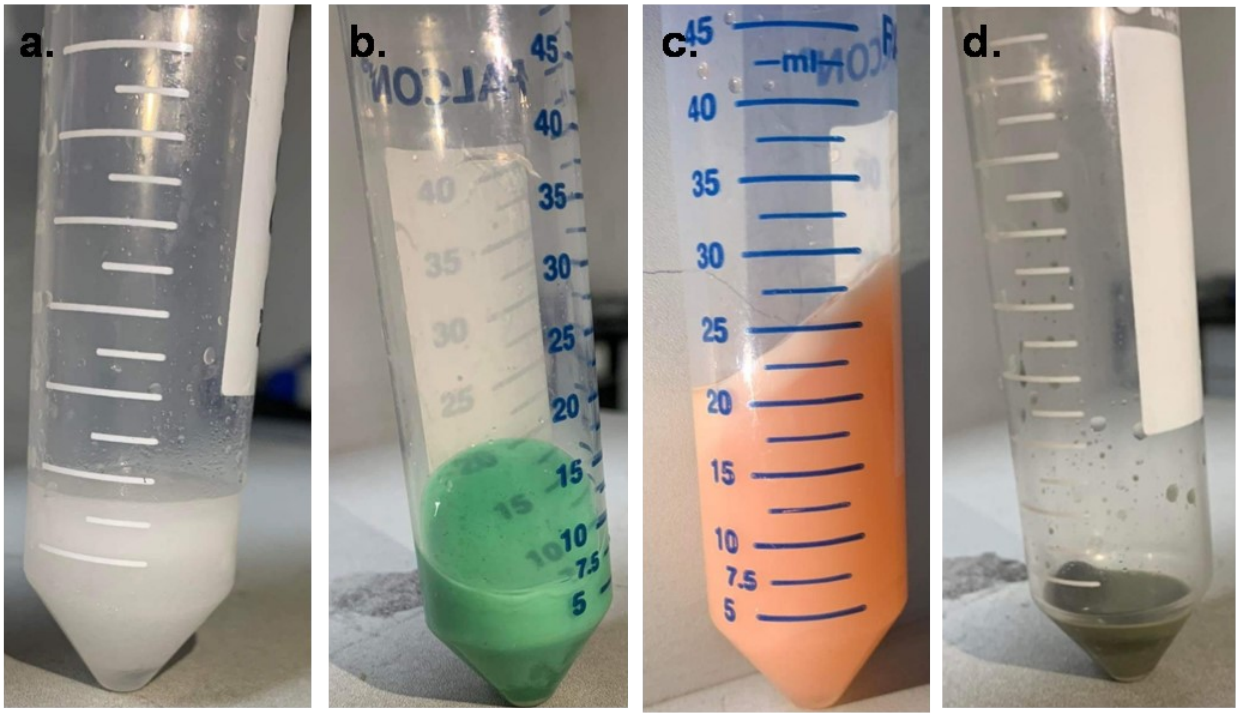

Figure S1. The photo images (a) PLGA NPs (blank), (b) ICG-loaded PLGA NPs, (c) Dox-loaded PLGA NPs and (d) Dox-ICG-loaded PLGA NPs during nanoparticles synthesis.

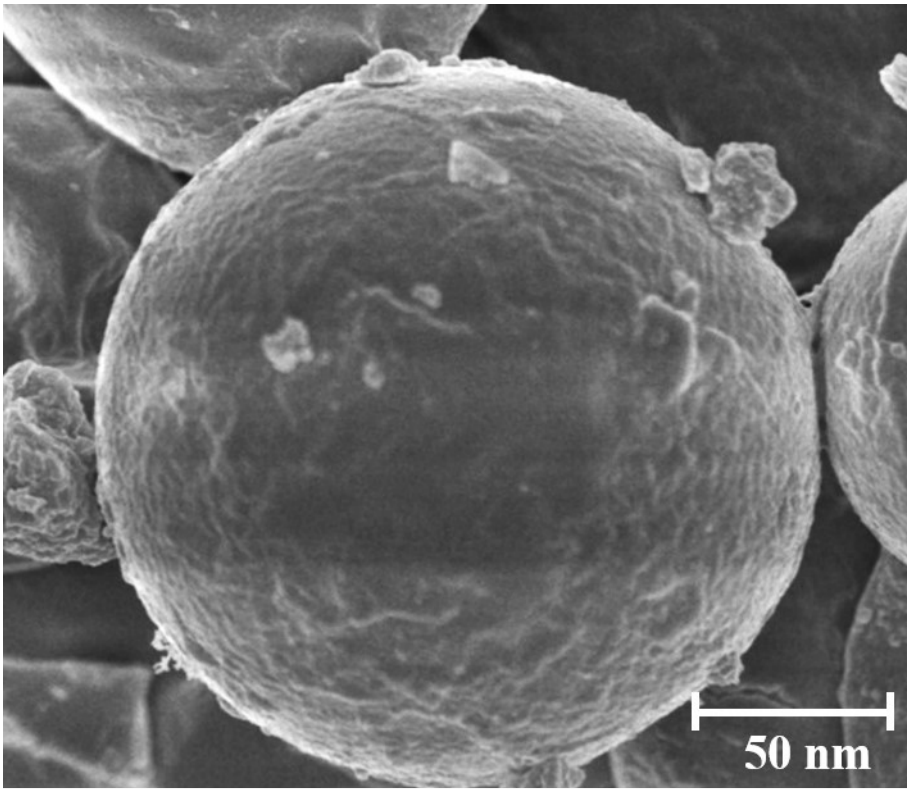

Figure S2. The magnified scanning electron microscopic (SEM) image (scale bar 50 nm) of Dox-ICG loaded PLGA NPs.

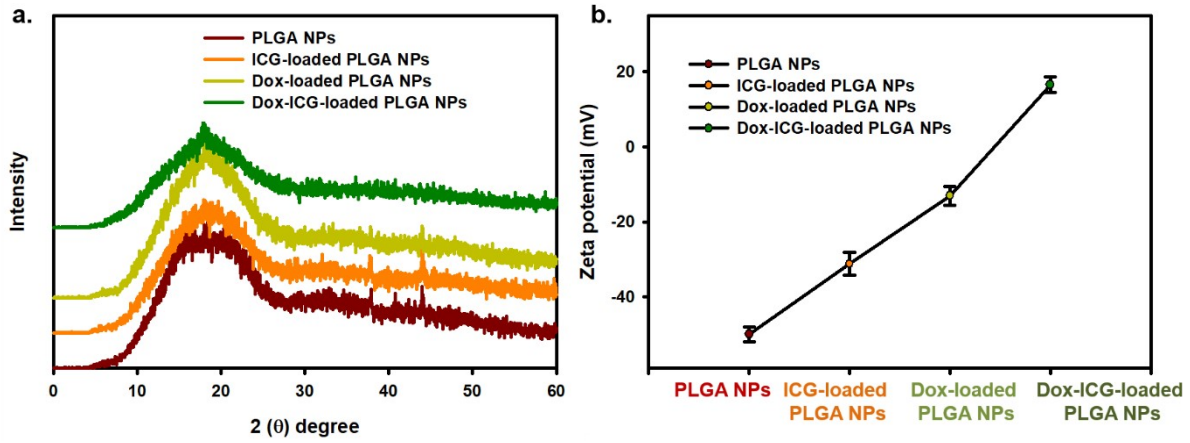

Figure S3. (a) The X-ray diffraction (XRD) pattern blank PLGA NPs, ICG-loaded PLGA NPs, Dox-loaded PLGA NPs and Dox-ICG-loaded PLGA NPs. (b) The zeta potential (mV) for the surface charge of PLGA NPs, ICG-loaded PLGA NPs, Dox-loaded PLGA NPs and (d) Dox-ICG-loaded PLGA NPs.

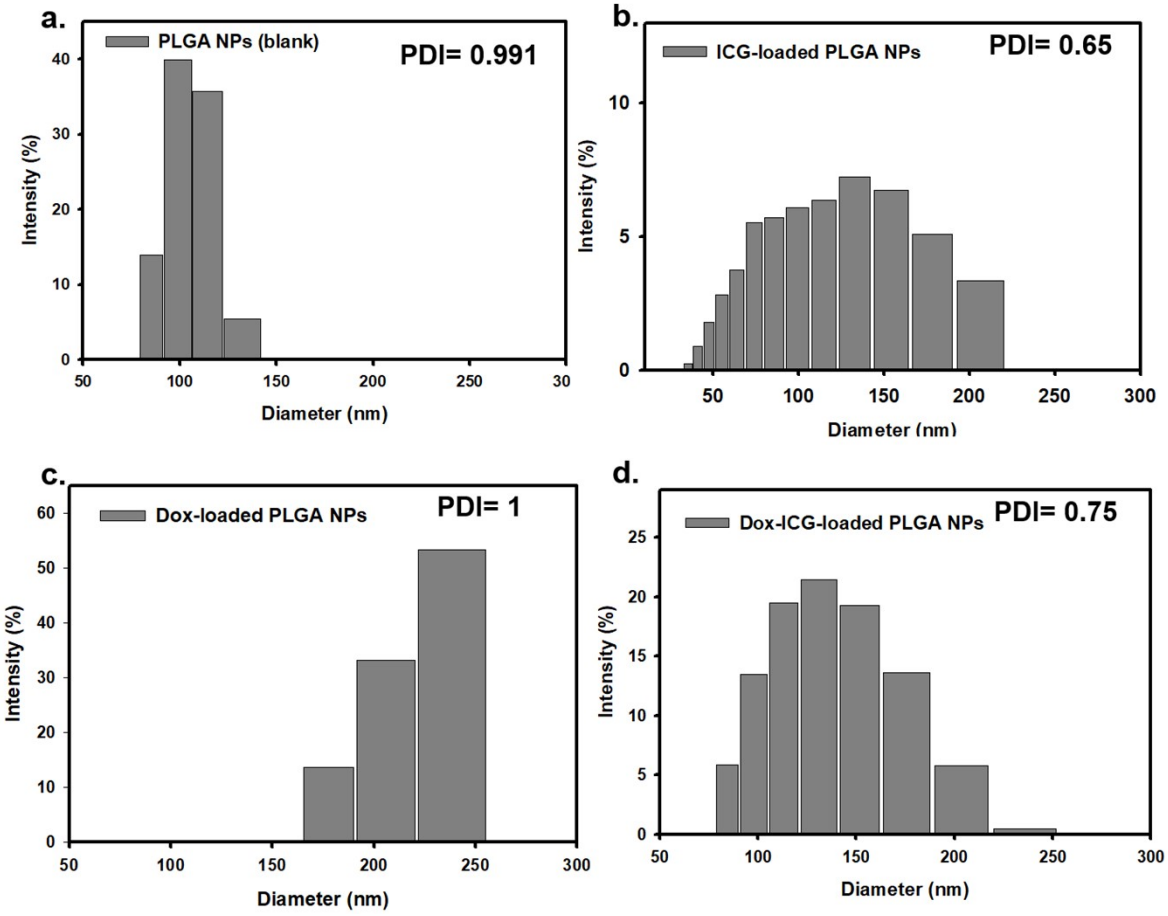

Figure S4. The dynamic light scattering (DLS) based hydrodynamic size (diameter) range and polydispersity index (PDI) analysis of (a) PLGA NPs, (b) ICG-loaded PLGA NPs, (c) Dox-loaded PLGA NPs and (d) Dox-ICG-loaded PLGA NPs.

The photothermal conversion efficiency was measured by using following equation:

$$\eta = \frac{hA\Delta T_{\max} - Q_s}{I(1 - 10^{-A\lambda})}$$

Where *h* is the heat transfer coefficient, *A* is the surface area of the container, Δ *T* max is the temperature change of the Dox-ICG-loaded PLGA NPs solution at the maximum steady-state temperature, *I* is the laser power, *A* λ is the Dox-ICG-loaded PLGA NPs at 808 nm, *Q* s is the heat associated with the light absorbance of the solvent, and η is the photothermal conversion efficiency. [1], [2]

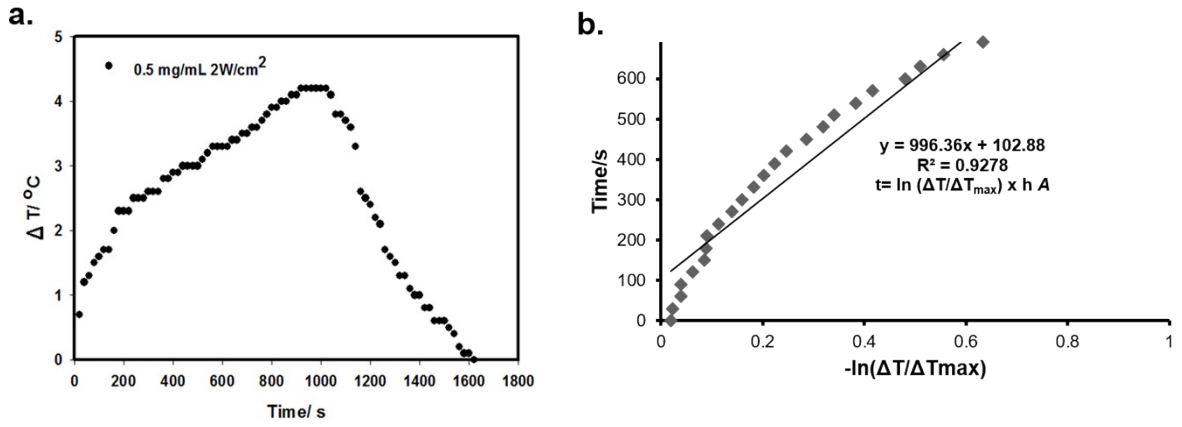

Figure S5. (Left) Temperature profile ($\Delta T=T_n-T_0$) of a solution of Dox-ICG-loaded PLGA NPs in water at 0.5 mg/mL when illuminated with a 808 nm laser (2 W/cm^2) during 15 min and after turning off the laser during 15 min; (Right) time constant for heat transfer is determined by applying the linear time from the cooling period (from 900 to 1600 s) versus negative natural logarithm of the driving force temperature.

References:

1. K. Mebrouk, F. Chotard, C. L. Goff-Gaillard, Y. Arlot-Bonnemains, M. Fourmigué, F. Camerel, Water-soluble nickel-bis(dithiolene) complexes as photothermal agents. *Chem. Commun.*, 2015, **51**, 5268-5270.

2. Sharker SM, Kim SM, Lee JE, Choi KH, Shin G, Lee S, Lee KD, Jeong JH, Lee H, Park SY. Functionalized biocompatible WO3 nanoparticles for triggered and targeted in vitro and in vivo photothermal therapy, *Journal of Controlled Release*, 2015, **217**, 211-220.

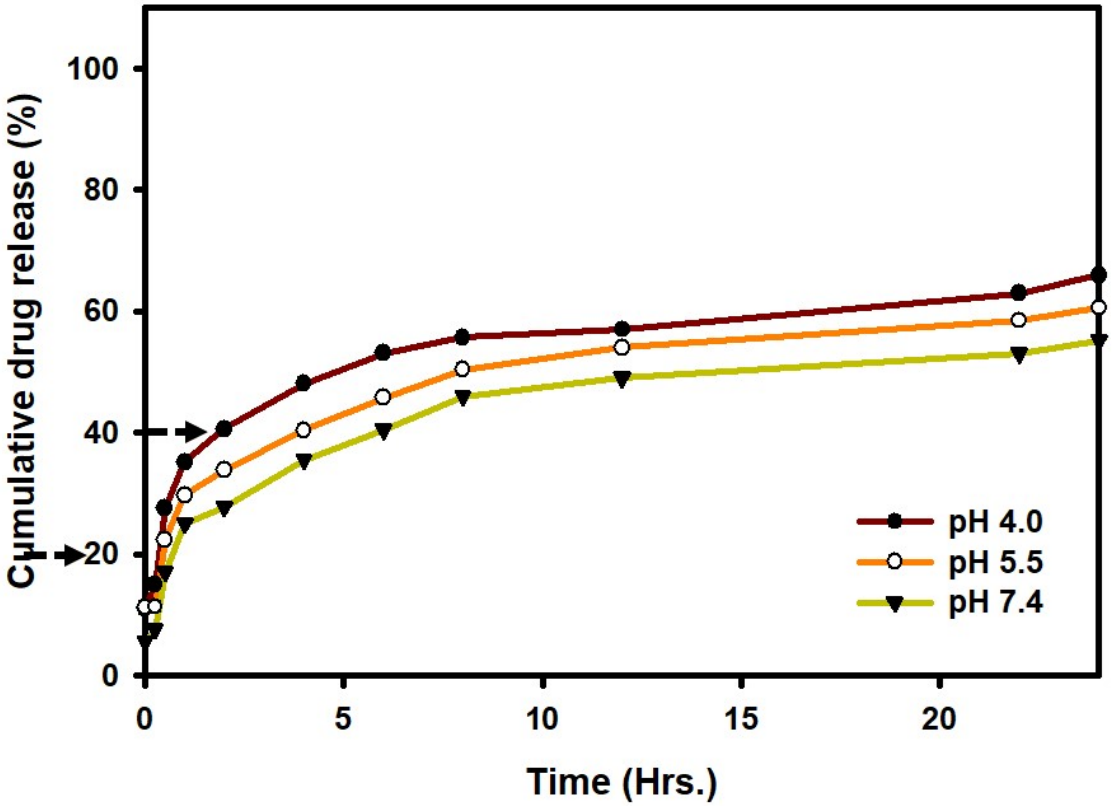

Figure S6. The pH-responsive in vitro (%) ICG release from Dox-ICG-loaded PLGA NPs. The release medium was pH 7.4, 5.5, and 4.0 with temperature 36°C. To determine the amount of ICG released, a 3 mL solution was taken from the outside released medium, and 3 ml of the solution was replaced by new-release media. The absorbances were measured at 810 nm using UV-visible spectroscopy; the amount (%) of the drug released was then calculated.

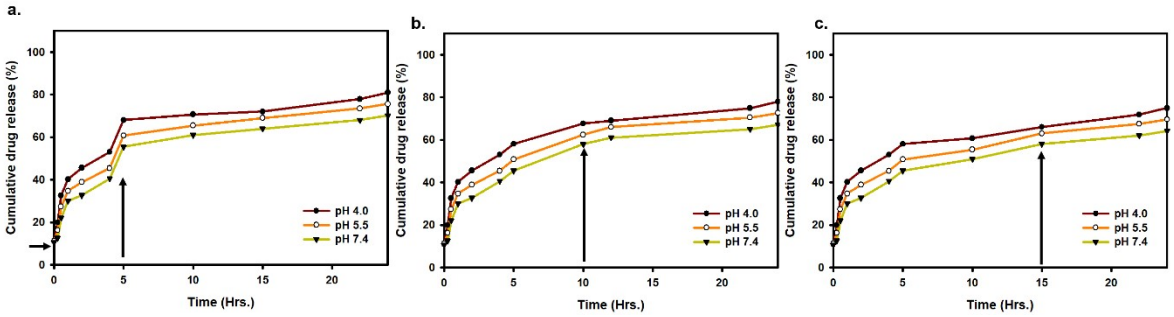

Figure S7. The heat-responsive *in vitro* drug release in response to 5 min NIR irradiation (808 nm laser, 2 W/cm2). The NIR light was used at the 5 h, (b) 10 h, (c) 15 h of drug release study.

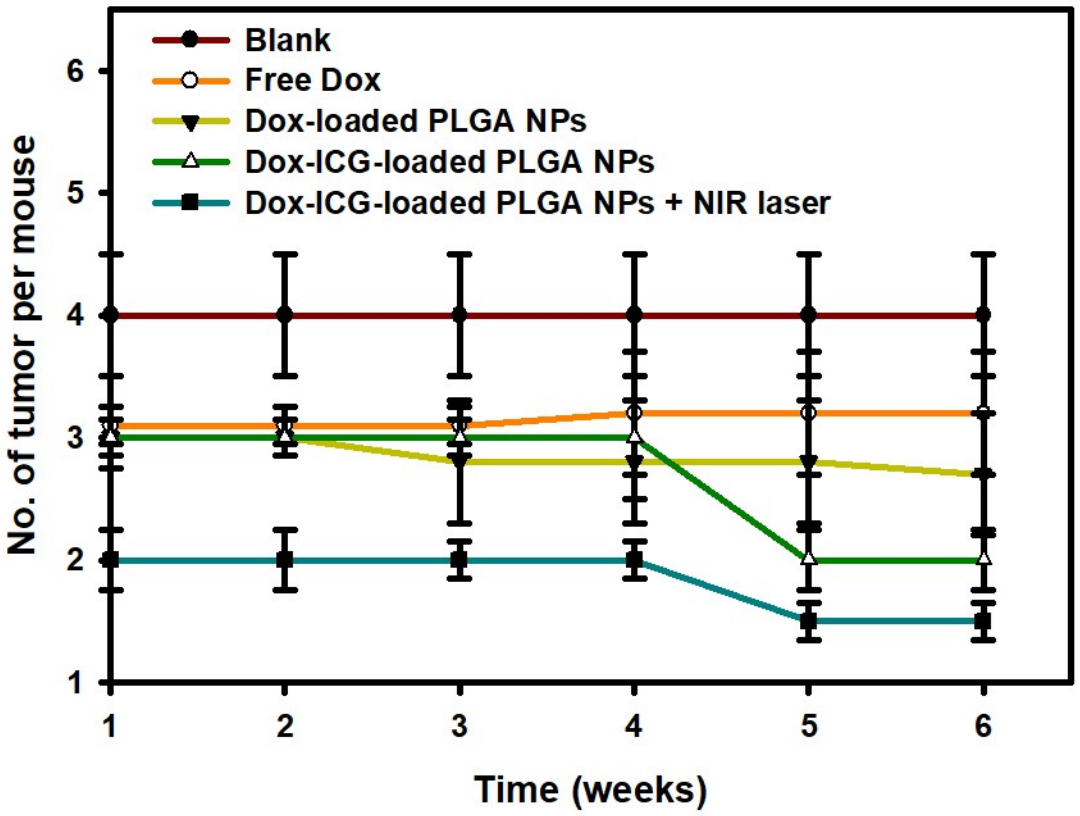

Figure S8. The *in vivo* anticancer activity by observing tumor number after administration of blank (control), free Dox, Dox-loaded PLGA NPs, Dox-ICG-loaded PLGA NPs and Dox-ICG-loaded PLGA NPs with 5 min NIR laser irradiation (mean ±SD, n = 5).

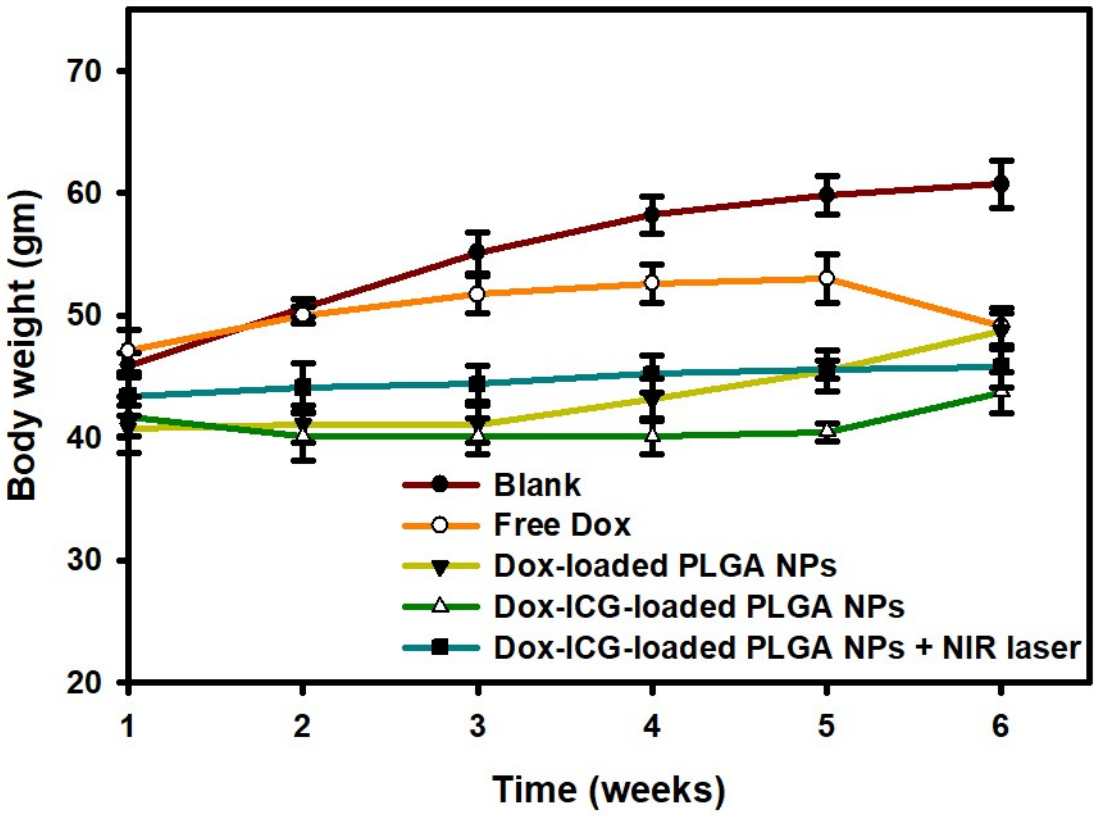

Figure S9. (a) The body (average) weight of the treated mice during in vivo anticancer activity of blank (control), free Dox, Dox-loaded PLGA NPs, Dox-ICG-loaded PLGA NPs and Dox-ICG-loaded-PLGA NPs with 5 min NIR laser irradiation (mean ±SD, n = 5).