Supporting Information

A Biomimetic Gold Nanocages-Based Nanoplatform for Efficient Tumor Ablation and Reduced Inflammation

Qingbo Xu[1], Jiangshan Wan[1], Nana Bie[1], Xianlin Song[2], Xiaoquan Yang[2], Tuying Yong[1], Yanbing Zhao[1], Xiangliang Yang[1,*], Lu Gan[1,*]

1. National Engineering Research Center for Nanomedicine, Hubei Key Laboratory of Bioinorganic Chemistry and Materia Medica, College of Life Science and Technology, Huazhong University of Science and Technology, Wuhan 430074, China
2. Britton Chance Center for Biomedical Photonics, Wuhan National Laboratory for Optoelectronics & Moe Key Laboratory of Biomedical Photonics of Ministry of Education, Department of Biomedical Engineering, Huazhong University of Science and Technology, Wuhan 430074, China

*Corresponding author: E-mail: lugan@mail.hust.edu.cn (L. Gan), yangxl@mail.hust.edu.cn (X. Yang)

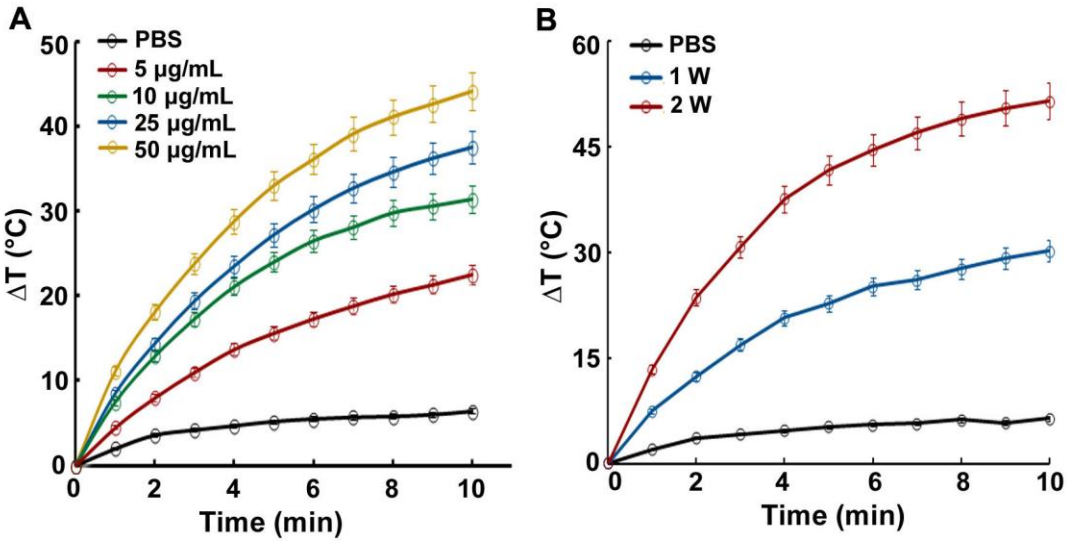

Figure S1. Concentration- and laser power-dependent photothermal effects of AuNCs. (**A, B**) Temperature rise profiles of AuNCs upon 808 nm laser irradiation at different concentrations at lase power of 1 W/cm^2 (**A**) or different laser power at the concentration of 25 μg/mL (**B**). Data as mean value ± SD (n=3).

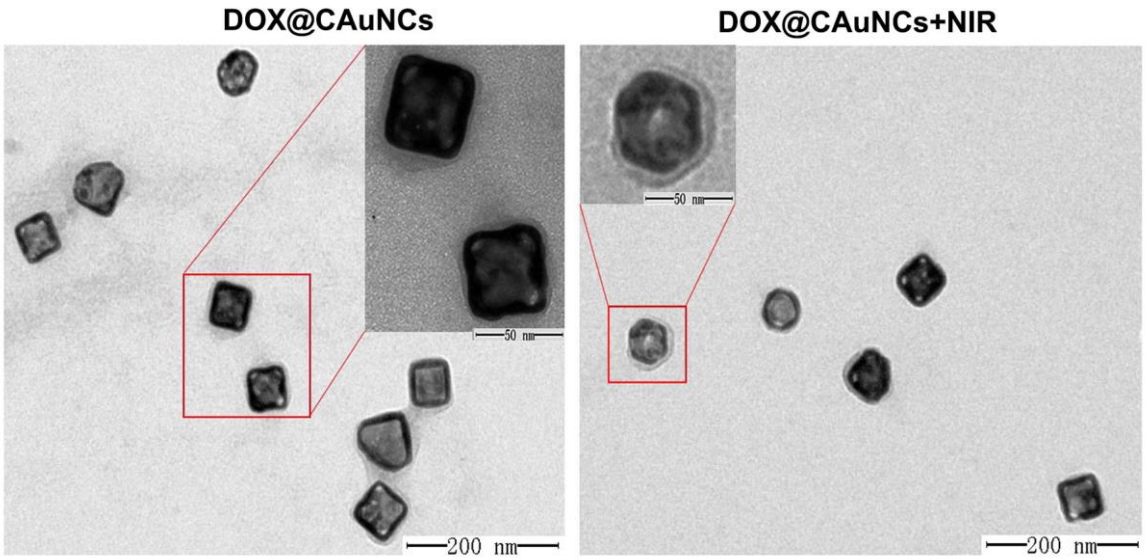

Figure S2. TEM images of DOX@CAuNCs in the presence or absence of 808 nm laser irraditaion (1 W/cm^2, 5 min).

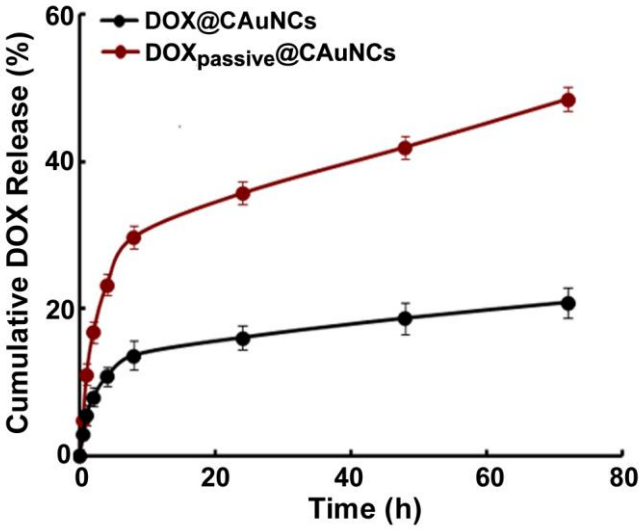

Figure S3. *In vitro* DOX release profiles from DOX@CAuNCs constructed using two different drug loading methods in PBS at pH 7.4. Data as mean value ± SD (n=3).

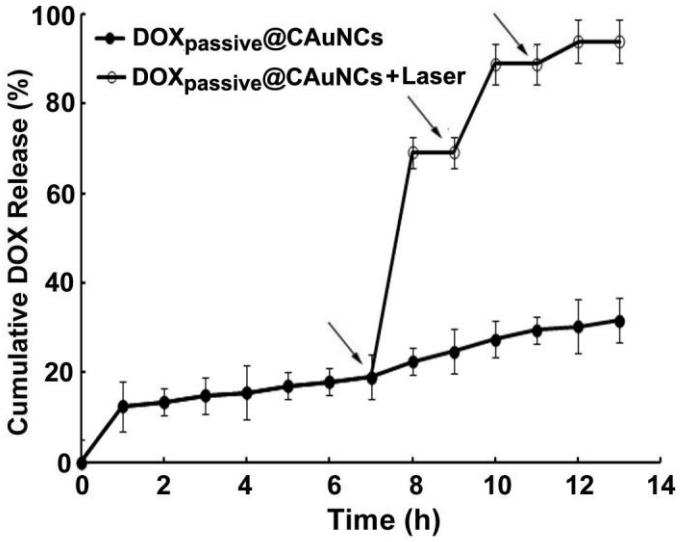

Figure S4. *In vitro* DOX release kinetics from $DOX_{passive}$@CAuNCs constructed using the passive drug loading method in PBS at pH 7.4 in the presence or absence of 808 nm laser irradiation (1 W/cm^2) for 5 min. Black arrows indicate the irradiation points. Data as mean value ± SD (n=3).

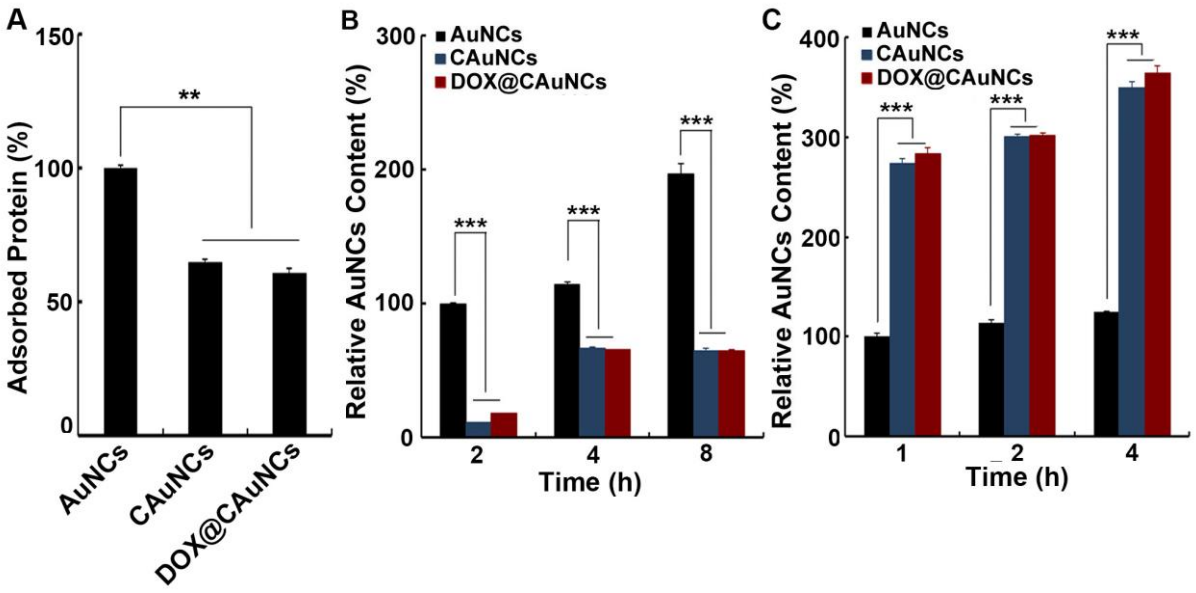

Figure S5. Effects of protein adsorption on macrophage phagocytosis and cellular uptake by cancer cells. (**A**) The adsorbsed FBS of AuNCs, CAuNCs and DOX@CAuNCs. (**B, C**) Intracellular Au content in RAW264.7 macrophages (**B**) and H22 cells (**C**) after treatment with AuNCs, CAuNCs or DOX@CAuNCs at Au concentration of 10 μg/mL in the presence of FBS for different time intervals. Data as mean value ± SD (n=4). ** P<0.01, *** P<0.001.

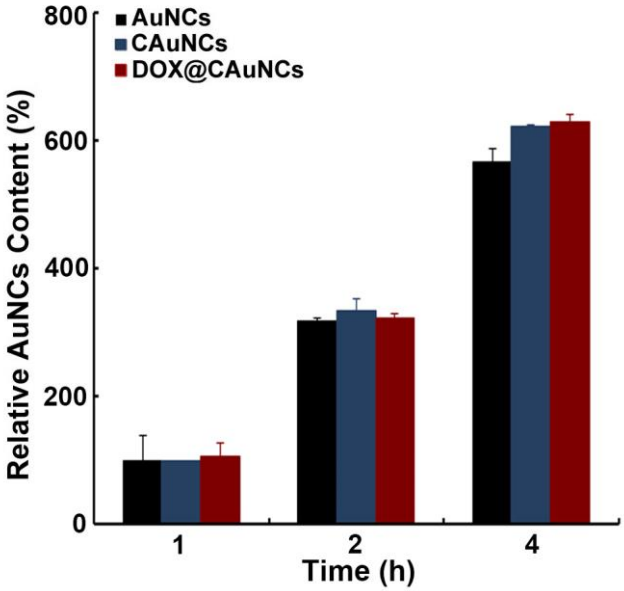

Figure S6. Intracellular Au content in NIH3T3 cells after treatment with AuNCs, CAuNCs or DOX@CAuNCs at Au concentration of 10 μg/mL in the presence of FBS for different time intervals. Data as mean value ± SD (n=4).

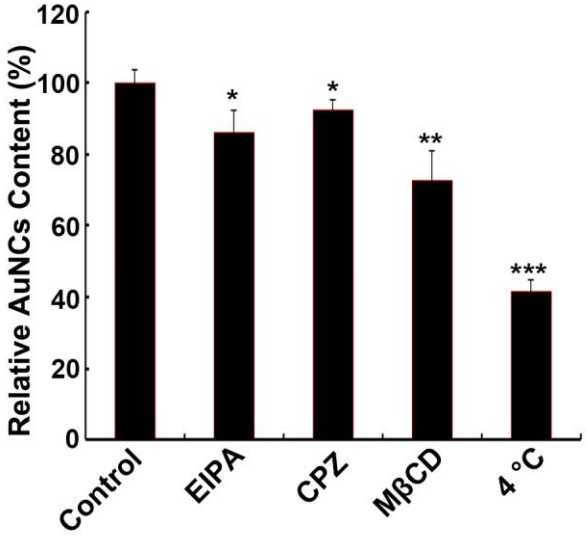

Figure S7. The intracellular Au contents in H22 cells pretreated with 50 μM EIPA, 10 μg/mL CPZ or 10 mM MβCD and then treated with DOX@CAuNCs at Au concentration of 10 μg/mL for 4 h. Data as mean value ± SD (n=4). **P*<0.05, ***P*<0.01, ****P*<0.001.

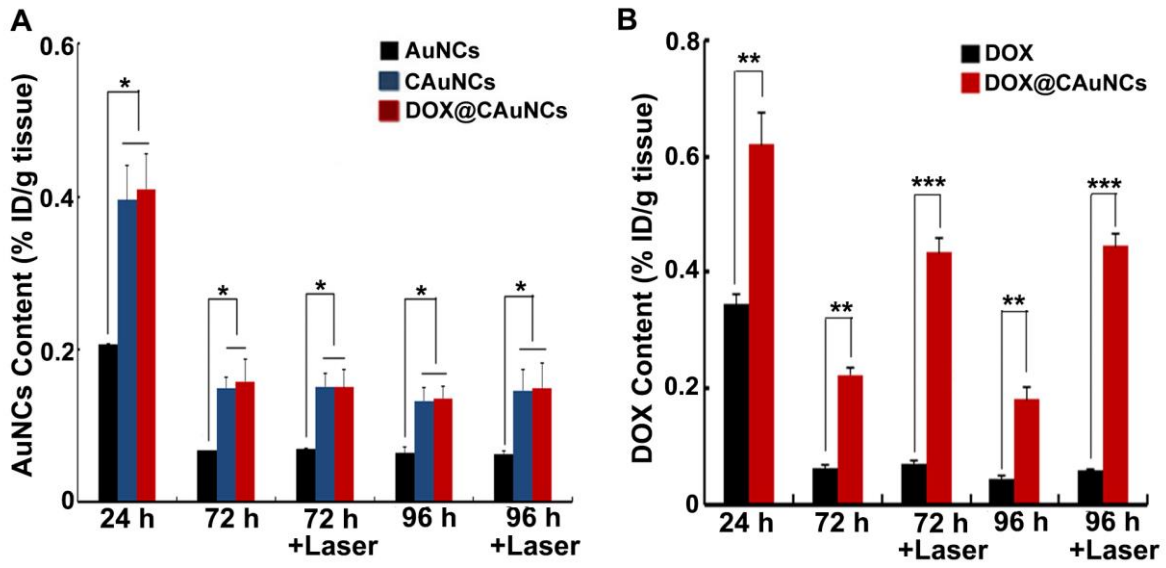

Figure S8. *In vivo* tumor retention of DOX@CAuNCs. (**A**) AuNCs contents in tumor tissues of H22 tumor-bearing at different time intervals after intravenous injection with AuNCs, CAuNCs or DOX@CAuNCs at Au dose of 10 mg/kg, followed with or without 808 nm laser irradiation (1 W/cm^2) for 10 min once a day at the tumor tissues. (**B**) DOX contents in tumor tissues of H22 tumor-bearing at different time intervals after intravenous injectin with free DOX or DOX@CAuNCs at DOX dose of 15 mg/kg, followed with or without 808 nm laser irradiation (1 W/cm^2) for 10 min once a day at the tumor tissues. Data as mean value ± SD (n=3). **P*<0.05, ***P*<0.01, ****P*<0.001.

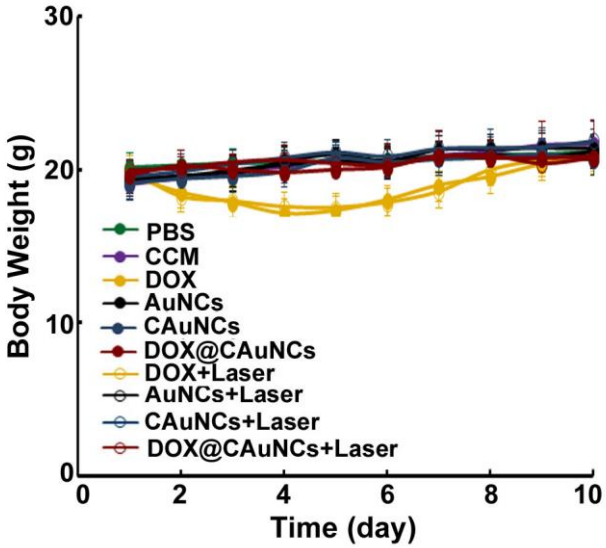

Figure S9. Body weight change of H22 tumor-bearing mice after intravenous injection with different formulations at the corresponding Au and DOX dose of 10 and 15 mg/kg, followed with or without 808 nm laser irradiation (1 W/cm^2) for 10 min once a day for four consecutive days at the tumor tissues. Data as mean value ± SD (n=13).

Table S1. Pharmacokinetic parameters of AuNCs, CAuNCs and DOX@CAuNCs in SD rats after intravenous administration at Au dose of 10 mg/kg (n=4).

Parameter	Units	AuNCs	CAuNCs	DOX@CAuNCs
$AUC_{(0-\infty)}$	mg/L*h	2761.3±312.6	5723.0±1708.2	5700.5±1094.9
$t_{1/2}$	h	20.06±0.27	35.82±9.79	34.06±5.2
CL	mL/h	0.724±7.76E-05	0.349±9.44E-05	0.351±6E-05

AUC: area under curve; $t_{1/2}$: plasma elimination half-life; CL: clearance.