Supporting Information

Tumor-Triggered Targeting Ammonium Bicarbonate Liposomes for Tumor Multimodal Therapy

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Materials

The cholesterol (Chol), 1,2-Dipalmitoyl-sn-glycero-3-phosphocholine (DPPC), and 1,2-distearylsn-glycero-3-phosphateethanolamine-N-(amino-(polyethyleneglycol)-2000) (DSPE-PEG_{2000}) were supplied by Avanti Polar Lipids (USA). The 1,2 - stearyl - sn - glycero - 3 - phosphatethanolamine (DSPE) and 1,2 - distearoyl - sn - glycero - 3 - phosphoethanolamine - N - [folate (polyethylene glycol) - 2000] (DSPE - PEG_{2000} - FA) were supplied by AVT (Shanghai, China). Doxorubicin hydrochloride (DOX) and indocyanine green (ICG) were supplied by Melonepharma (Dalian, China). Methoxy PEG_{5000} propionaldehyde ($mPEG_{5000}$ - CHO) was supplied by JenKem Technology (Beijing, China), and other chemicals were supplied by Sinopharm Chemical Reagent Co. Ltd, China.

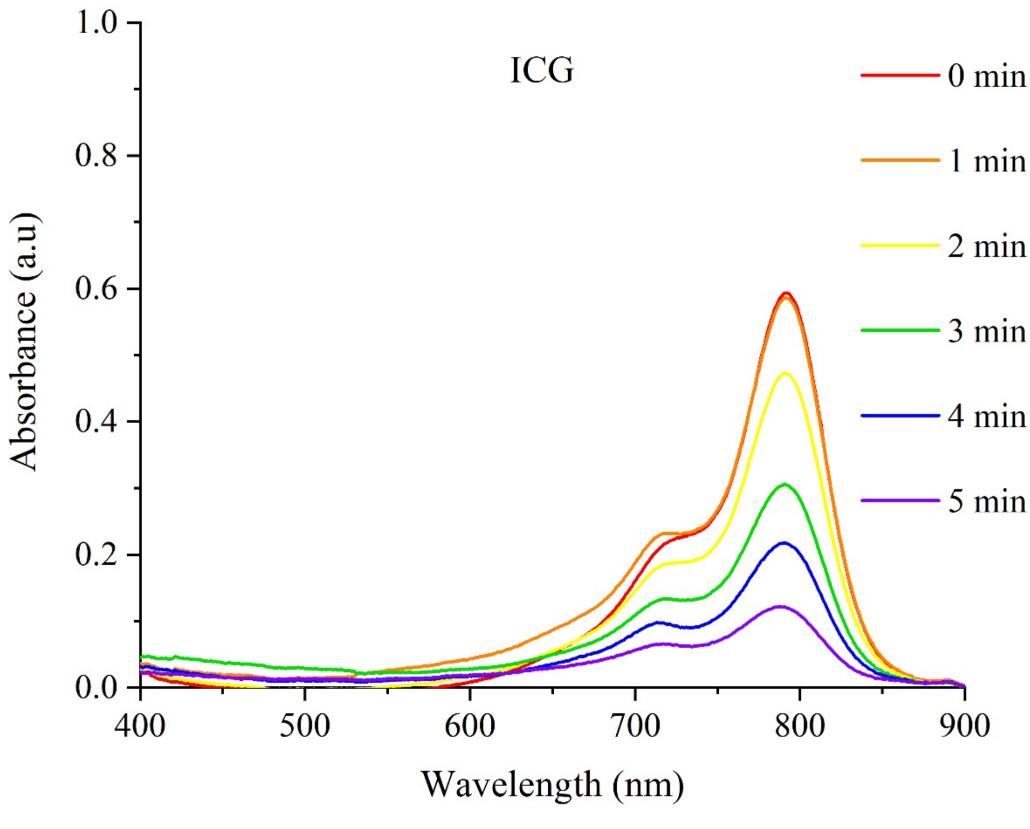

Figure S1 UV-visible absorption spectra of free ICG

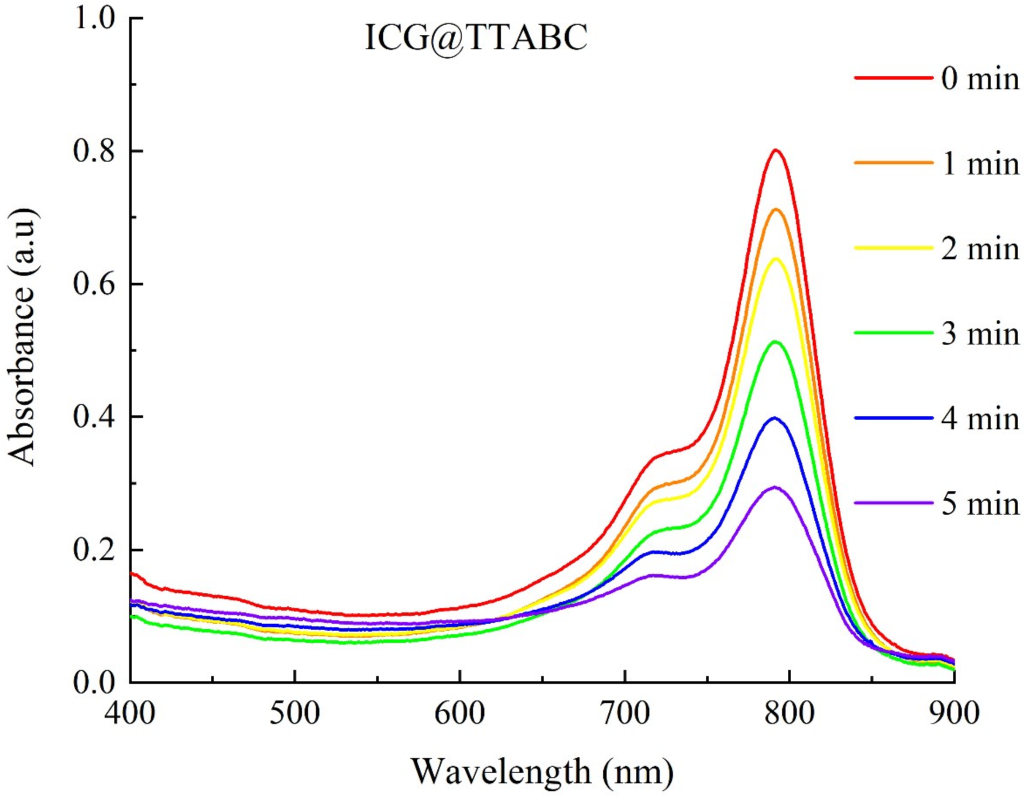

Figure S2 UV-visible absorption spectra of ICG@TTABC

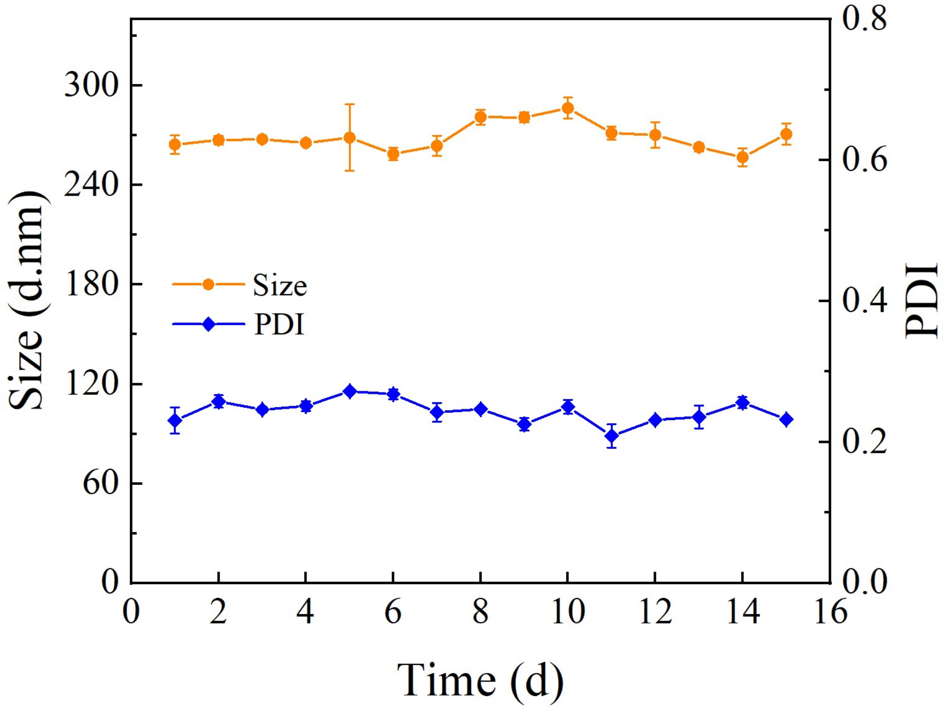

Figure S3 Hydrodynamic size of ICG&DOX@TTABC within 15 days

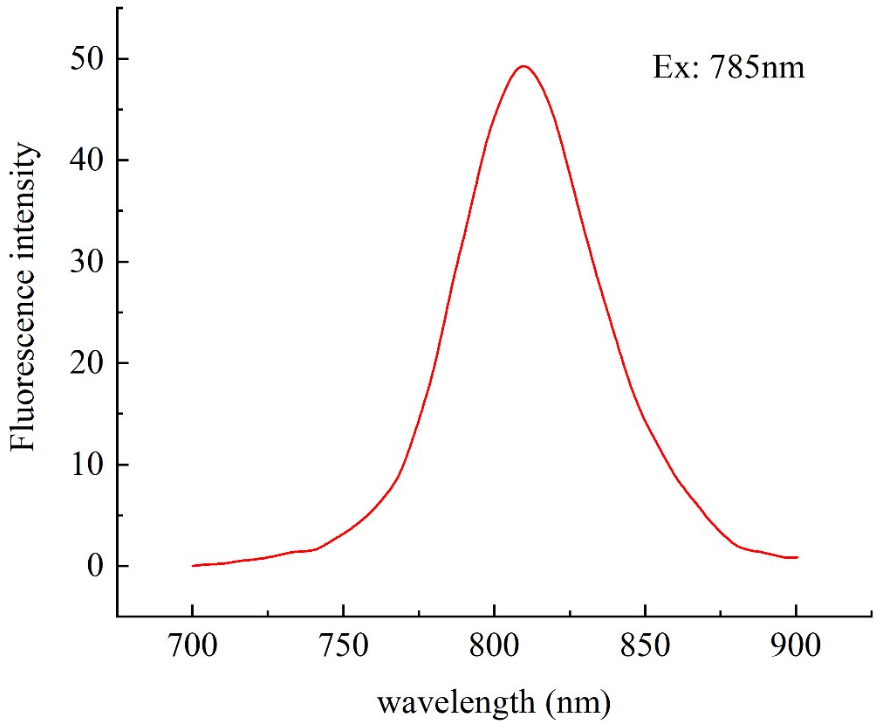

Figure S4 Fluorescence emission spectrum of ICG

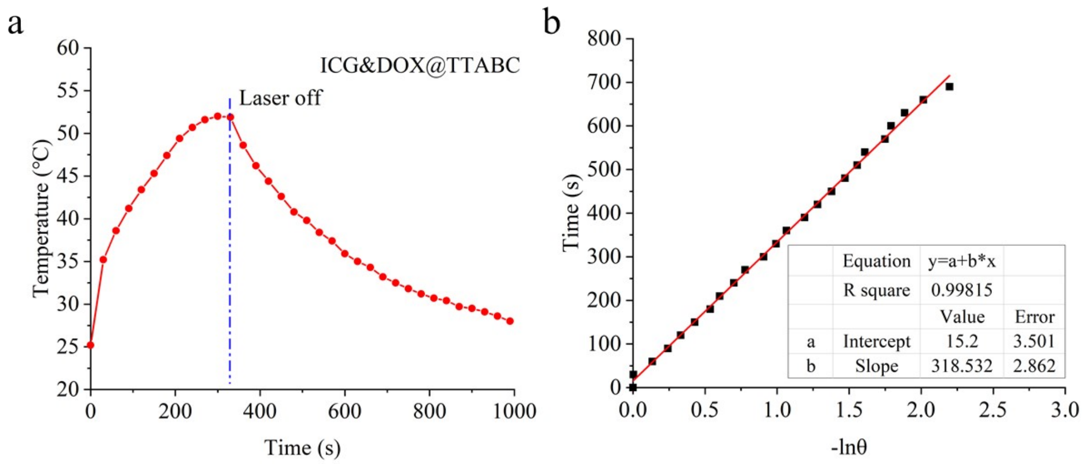

Figure S5 a) The photothermal response of the ICG&DOX@TTABC aqueous solution irradiated with NIR laser (808 nm, 1.5 W/cm^2) for 330 s, and then the laser was shut off. b) Linear time data *versus* Lnθ obtained from the cooling period of panel.

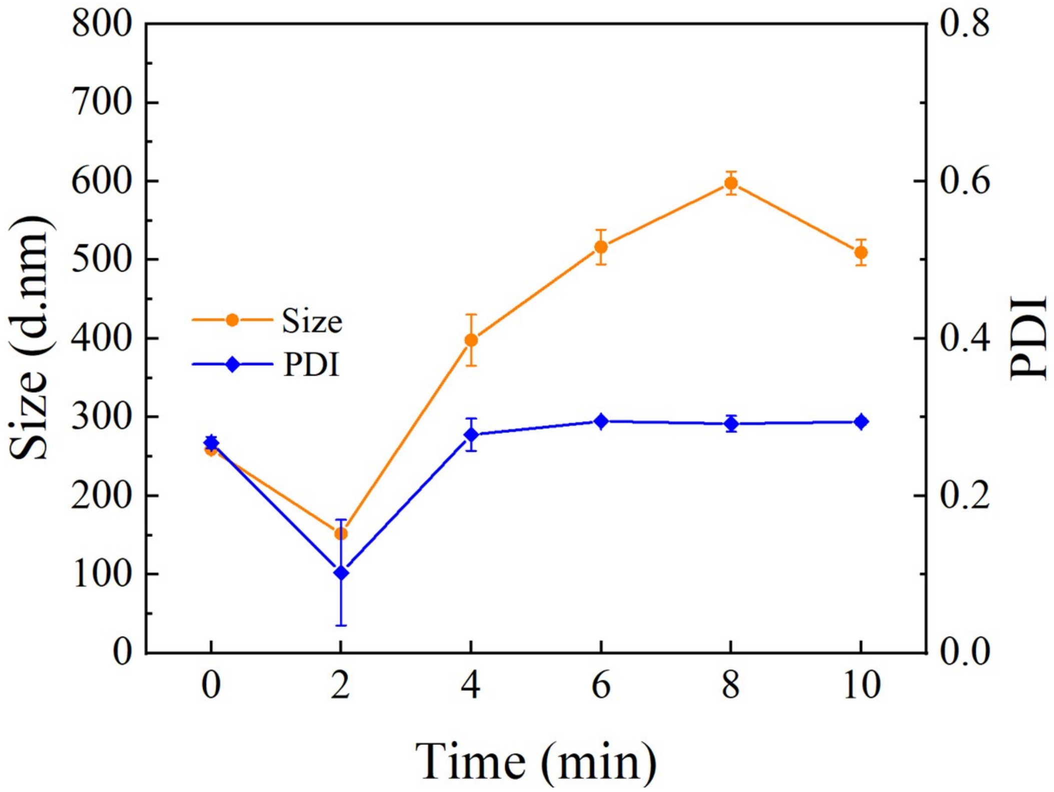

Figure S6 Hydrodynamic size of ICG&DOX@TTABC *versus* irradiation time (808 nm, 1.5 W/cm^2)

Calculation of the photothermal conversion efficiency

The photothermal conversion efficiency of ICG&DOX@TTABC was determined according to previous method.[1-3]

$$\sum_i m_i c_{i,p} \frac{dT}{dt} = Q_{NCs} + Q_{Dis} - Q_{Surr} \quad (1)$$

where m and $C_{i,p}$ are the mass and heat capacity of water, respectively. T is the solution temperature, Q_{NCs} is the energy inputted by ICG&DOX@TTABC, Q_{Dis} is the baseline energy inputted by the sample cell, and Q_{Surr} is heat conduction away from the system surface by air.

Q_{NCs} is the photothermal energy input by ICG&DOX@TTABC.

$$Q_{NCs} = I(1 - 10^{-A_\lambda})\eta \quad (2)$$

where I is incident laser power, η is the conversion efficiency from incident laser energy to thermal energy, and A_λ is the absorbance of the ICG&DOX@TTABC at wavelength of 808 nm. In addition, source term, Q_{Dis} is the heat associated with the light absorbance of the solvent, which is measured independently to be Q_{Dis} = 18.9 mW using pure water without ICG&DOX@TTABC. Furthermore, Q_{Surr} is thermal energy lost to the surroundings.

$$Q_{Surr} = hS(T - T_{Surr}) \quad (3)$$

where h is heat transfer coefficient, S is the surface area of the container, and T_{Surr} is ambient temperature of the surroundings.

Once the laser power is defined, the heat input (Q_{NC} + Q_{Dis}) will be finite. Since the heat output (Q_{Surr}) is increased along with the increase of the temperature according to the Eq.3, the system temperature will rise to a maximum when the heat input is equal to heat output:

$$Q_{NCs} + Q_{Dis} = Q_{Surr-max} = hS(T - T_{Surr}) \quad (4)$$

where the $Q_{Surr\text{-}Max}$ is heat conduction away from the system surface by air when the sample cell reaches the equilibrium temperature, and T_{max} is the equilibrium temperature. The 808 nm laser heat conversion efficiency (η) can be determined by substituting Eq.2 for Q_{NCs} into Eq. 4 and rearranging to get

$$\eta = \frac{hS(T - T_{Surr}) - Q_{Dis}}{I(1 - 10^{-A_\lambda})} \quad (5)$$

where Q_{Dis} was measured independently to be 18.9 mW, the (T_{max}-T_{Surr}) was 27.0 °C according to Figure S5a, I is 1.5 W/cm^2, A_{808} is the absorbance (0.6390) of ICG&DOX@TTABC at 808 nm (Figure 2e). Thus, only the hS remains unknown for calculating η

In order to get the hS, a dimensionless driving force temperature, θ is introduced using the maximum system temperature, T_{max}

$$\theta = \frac{T - T_{Surr}}{T_{max} - T_{Surr}} \quad (6)$$

Substituting Eq.6 into Eq.1 and rearranging Eq.1

$$\frac{d\theta}{dt} = \frac{hS}{\sum_i m_i c_{i,p}}\left[\frac{Q_{NCs} + Q_{Dis}}{hS(T_{max} - T_{Surr})} - \theta\right] \quad (7)$$

When the laser was shut off, the Q_{NCs}+ Q_{Dis} = 0, Eq.7 changed to

$$dt = \frac{\sum_i m_i c_{i,p}}{hS}\frac{d\theta}{\theta} \quad (8)$$

and integrating, giving the expression

$$t = -\frac{\sum_i m_i c_{i,p}}{hS}\ln\theta \quad (9)$$

Therefore, time constant for heat transfer from the system is determined to be $\frac{\sum_i m_i c_{i,p}}{hS}$ = 318.532 s by applying the linear time data from the cooling period (after 330 s) *vs* negative natural logarithm of driving force temperature (Figure S5b). In addition, the m is 1.0 g and the C is 4.2 *J/(g ℃)*. Thus, according to Eq. 9, the hS is deduced to be 13.18 *mW/°C*. Substituting13.18 *mW/°C* of the hS into Eq.5, the 808 nm laser heat conversion efficiency (η) of ICG&DOX@TTABC can be calculated to be 29.16%.

References

1. M. B. Zheng, P. F. Zhao, Z. Y. Luo, P. G, C. F. Zheng, P. F. Zhang, C. X. Yue, D. Y Gao, Y. F. Ma and L. T. Cai, Robust ICG theranostic nanoparticles for folate targeted cancer imaging and highly effective photothermal therapy, *ACS Appl. Mater. Interfaces,* 2014, **6**, 6709−6716.

2. Q. W. Tian, F. R. Jiang, R. J. Zou, Q. Liu, Z. G. Chen, M. F. Zhu, S. P. Yang, J. L. Wang, J. H. Wang and J. Q. Hu, Hydrophilic Cu9S5 nanocrystals: a photothermal agent with a 25.7% heat conversion efficiency for photothermal ablation of cancer cells in *vivo*, *ACS Nano*, 2011, **5**, 9761−9771.

3. H. T. Bi, Y. L. Dai, J. T. Xu, R. C. Lv, F. He, S. L. Gai, D. Yang and P. P. Yang, CuS-Pt (IV)-PEG-FA nanoparticles for targeted Photothermal and chemo-therapy, *J. Mater. Chem. B,* 2016, **4**, 5938-5946.