

## Electronic Supplementary Information

### Design of Raman tag-bridged core-shell Au@Cu<sub>3</sub>(BTC)<sub>2</sub> nanoparticles for Raman imaging and synergistic chemo-photothermal therapy

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### Calculation of the photothermal conversion efficiency.

1 mL aqueous dispersion of Au@Cu<sub>3</sub>(BTC)<sub>2</sub> NPs (100 µg mL<sup>-1</sup>) were moved into a cuboid well, and irradiated under an 808 nm NIR laser at a power density of 2 W cm<sup>-2</sup> for 600 s. The temperature of the dispersion was measured every 30 s after the start of irradiation (**Figure S12a**). After the laser irradiation was shut off, the temperature was further measured for another 1200 s with the same intervals (**Figure S12b**). Ultrapure water as control group was treated under the same conditions.

The photothermal conversion efficiency ( $\eta$ ) of Au@Cu<sub>3</sub>(BTC)<sub>2</sub> NPs was calculated according to previous reports<sup>1</sup>. The detailed calculation was carried out as following equations:

The total energy balance of this system as following equation:

$$\sum_i m_i C_{p,i} \frac{dT}{dt} = Q_{NPs} + Q_s - Q_{loss} \quad (1)$$

where  $m$  and  $C_p$  are the mass and heat capacity, respectively. The suffix “ $i$ ” of  $m$  and  $C_p$  refers to solvent (water) or dispersed matter (nanoparticles).  $T$  is the solution temperature.

$Q_{NPs}$  is the photothermal energy absorbed by Au@Cu<sub>3</sub>(BTC)<sub>2</sub> NPs per second:

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

where  $I$  is the laser power,  $A_\lambda$  is the absorbance of Au@Cu<sub>3</sub>(BTC)<sub>2</sub> NPs at the wavelength of 808 nm in aqueous solution, and  $\eta$  is the photothermal conversion efficiency of Au@Cu<sub>3</sub>(BTC)<sub>2</sub> NPs which means the ratio of absorbed light energy converting to thermal energy.

$Q_{loss}$  is thermal energy lost to the surroundings:

$$Q_{loss} = hA\Delta T \quad (3)$$

Where  $h$  is the heat transfer coefficient,  $A$  is the surface area of the container, and  $\Delta T$  is the changed temperature, which is referred to  $T - T_{surr}$  ( $T$  and  $T_{surr}$  are the solution temperature and ambient temperature of the surrounding, respectively).

$Q_s$  is the heat associated with the light absorbed by solvent per second. In the situation of heating pure water, the heat input is equal to the heat output at the maximum steady-state temperature, so the equation can be:

$$Q_s = Q_{loss} = hA\Delta T_{max, H_2O} \quad (4)$$

Where  $\Delta T_{max, H_2O}$ , is the temperature change of water at the maximum steady-state temperature. As it to the experiment of Au@Cu<sub>3</sub>(BTC)<sub>2</sub> NPs dispersion, the heat inputs are the heat generated by nanoparticles( $Q_{NPs}$ ) and the heat generated by water( $Q_s$ ), which is equal to the heat output at the maximum steady-state temperature, so the equation can be:

$$Q_{NPs} + Q_s = Q_{loss} = hA\Delta T_{max, mix} \quad (5)$$

Where  $\Delta T_{max, mix}$  is the temperature change of the Au@Cu<sub>3</sub>(BTC)<sub>2</sub> NPs dispersion at the maximum steady-state temperature. According to the equation (2), (4) and (5), the photothermal conversion efficiency ( $\eta$ ) can be expressed as following:

$$\eta = \frac{hA\Delta T_{max, mix} - hA\Delta T_{max, H_2O}}{I(1 - 10^{-A\lambda})} = \frac{hA(\Delta T_{max, mix} - \Delta T_{max, H_2O})}{I(1 - 10^{-A\lambda})} \quad (6)$$

In this equation, only  $hA$  is unknown. In order to get the  $hA$ , we introduce  $\theta$ , which is

defined as the ratio of  $\Delta T$  to  $\Delta T_{max}$ :

$$\theta = \frac{\Delta T}{\Delta T_{max}} \quad (7)$$

Substituting equation (7) into equation (1):

$$\frac{d\theta}{dt} = \frac{hA}{\sum_i m_i C_{p,i}} \left[ \frac{Q_{NPs} + Q_s}{hA\Delta T_{max}} - \theta \right] \quad (8)$$

When the laser was shut off, the  $Q_{NPs} + Q_s = 0$ , equation (8) could be expressed to:

$$dt = - \frac{\sum_i m_i C_{p,i}}{hA} \frac{d\theta}{\theta} \quad (9)$$

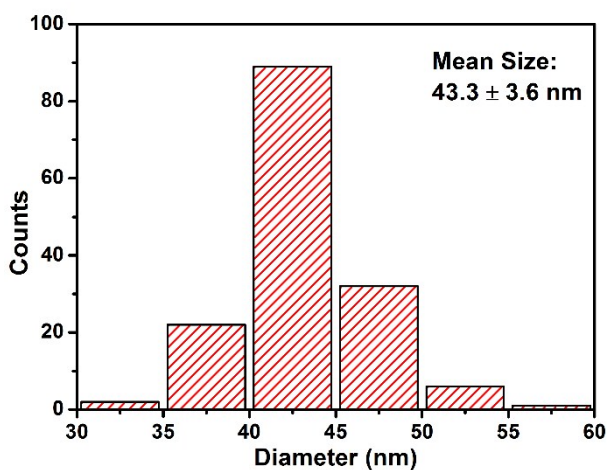
Equation (9) changes the expression:

$$t = - \frac{\sum_i m_i C_{p,i}}{hA} \ln\theta \quad (10)$$

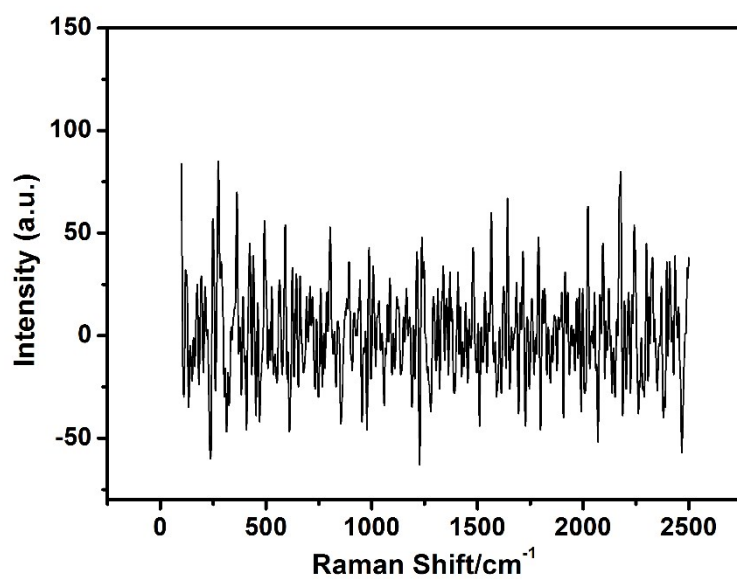
Where  $\frac{\sum_i m_i C_{p,i}}{hA}$  can be calculated by linear relationship of time versus  $-\ln(\theta)$  (**Figure S12c**). Compared with solvent (water,  $1 \times 10^{-3}$  Kg), mass of NPs ( $1 \times 10^{-7}$  Kg) was too little. Generally, the specific heat of water is much higher than other materials. Consequently, the  $m_{NPs}$  and  $C_{p,NPs}$  of NPs were neglected.  $m_{H_2O}$  was  $1 \times 10^{-3}$  Kg.  $C_p$ ,  $H_2O$  was  $4.2 \times 10^3$  J Kg $^{-1}$ . So we can get  $hA$  equals 0.0132.

Now go back to equation 6 again, every parameter is clear now.  $\Delta T_{max,mix}$  was 41.3.  $\Delta T_{max,H_2O}$  is 4.4.  $I$  was 2.0 W where the area of light spot was 1.0 cm $^2$ .  $A_\lambda$  (808 nm)

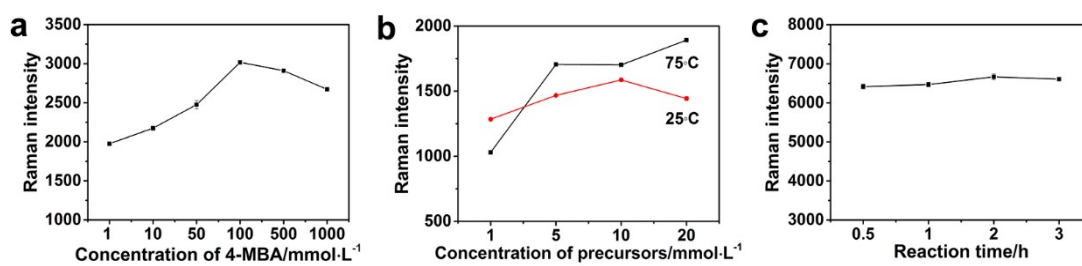
was 0.662 (**Figure S12d**). Thus, the photothermal conversion efficiency ( $\eta$ ) of Au@Cu<sub>3</sub>(BTC)<sub>2</sub> NPs was calculated to be 31.2%.



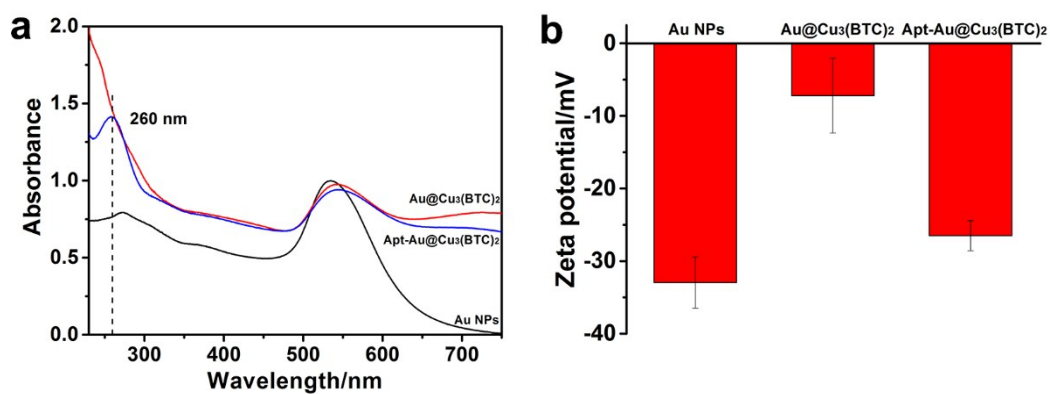
**Figure S1** The corresponding Au@Cu<sub>3</sub>(BTC)<sub>2</sub> NPs size distribution with one cycle time, the total number of NPs for statistics is 152.



**Figure S2** Raman spectra of  $\text{Cu}_3(\text{BTC})_2$  (3 mg/mL) mixed with Au NPs with a volume ratio of 1:1.

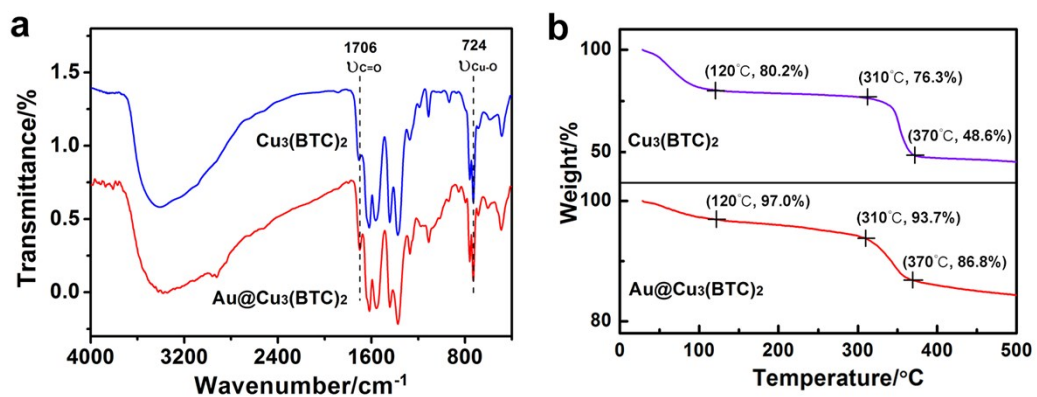


**Figure S3** Influence of concentrations of 4-MBA (a), concentrations of precursors at 75°C (black) and 25°C (red) (b), and reaction time (c) on Raman intensity.

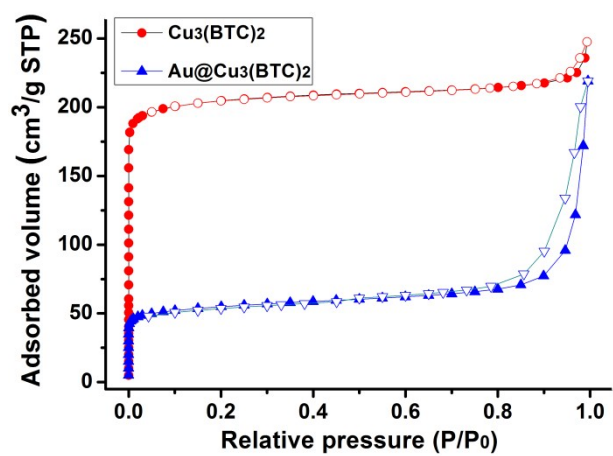


**Figure S4** UV-vis spectra (a) and zeta potential (b) of Au NPs, Au@Cu<sub>3</sub>(BTC)<sub>2</sub> NPs and aptamer modified Au@Cu<sub>3</sub>(BTC)<sub>2</sub> NPs (Apt-Au@Cu<sub>3</sub>(BTC)<sub>2</sub> NPs).





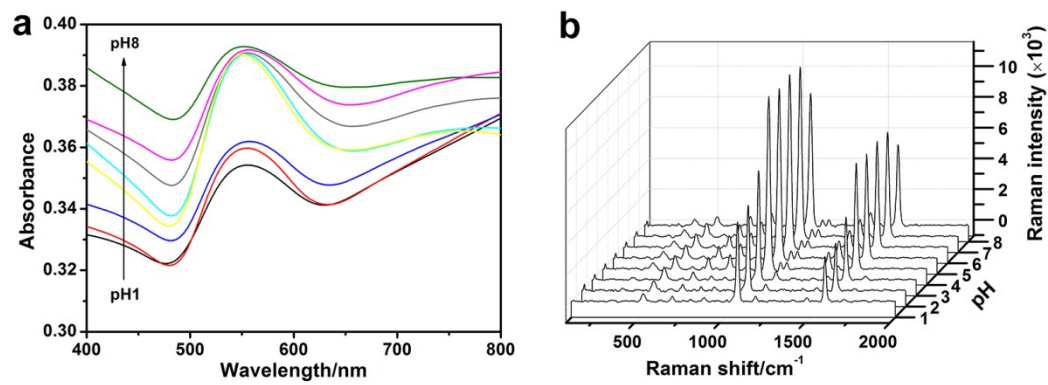
**Figure S5** (a) Infrared spectra of  $Cu_3(BTC)_2$  and  $Au@Cu_3(BTC)_2$ , and (b) TGA curves of  $Cu_3(BTC)_2$  and  $Au@Cu_3(BTC)_2$  under nitrogen flow.



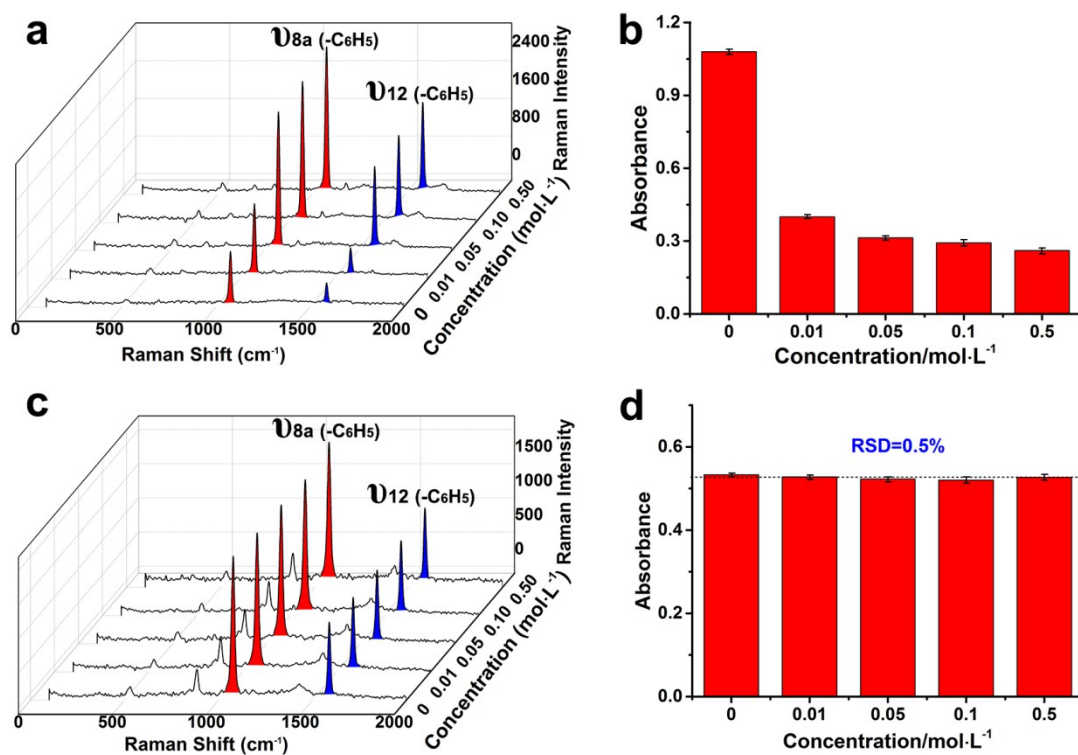
**Figure S6** N<sub>2</sub> adsorption-desorption isotherms of Cu<sub>3</sub>(BTC)<sub>2</sub> and Au@Cu<sub>3</sub>(BTC)<sub>2</sub>.

**Table S1** List of surface areas, pore volume and average pore sizes of  $\text{Cu}_3(\text{BTC})_2$  and  $\text{Au}@\text{Cu}_3(\text{BTC})_2$ .

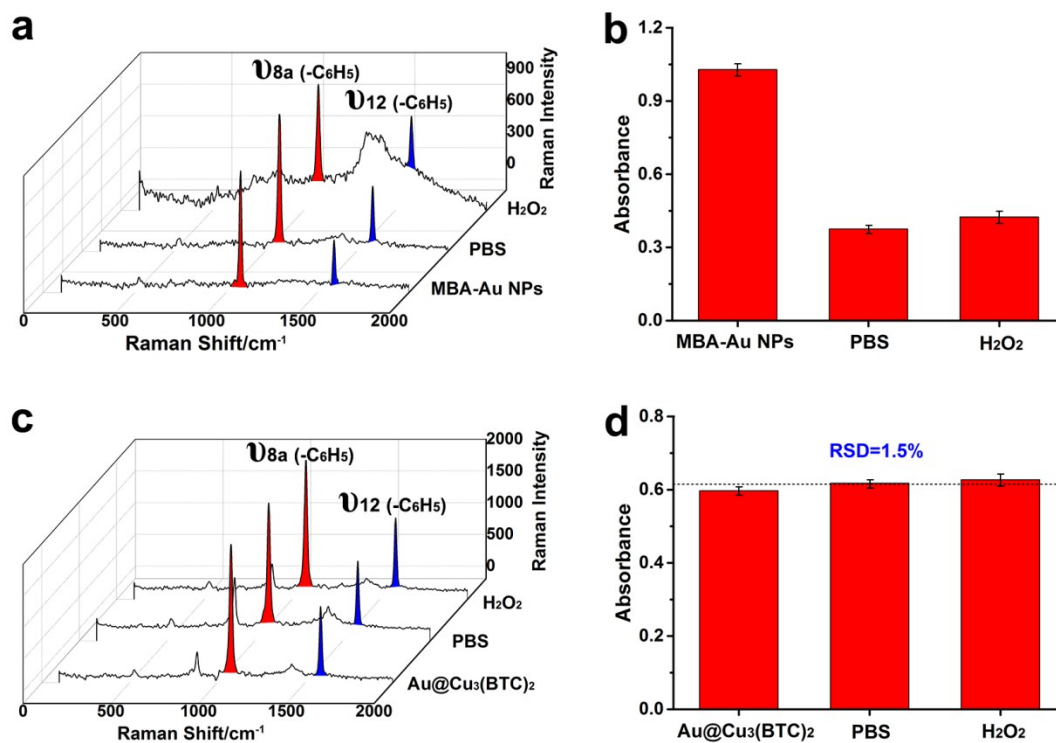
Samples	BET Surface Area ( $\text{m}^2\cdot\text{g}^{-1}$ )	Pore Volume ( $\text{cm}^3\cdot\text{g}^{-1}$ )	Average Pore Size ( $\text{\AA}$ )
$\text{Cu}_3(\text{BTC})_2$	823	0.383	8.57
$\text{Au}@\text{Cu}_3(\text{BTC})_2$	207	0.339	8.99



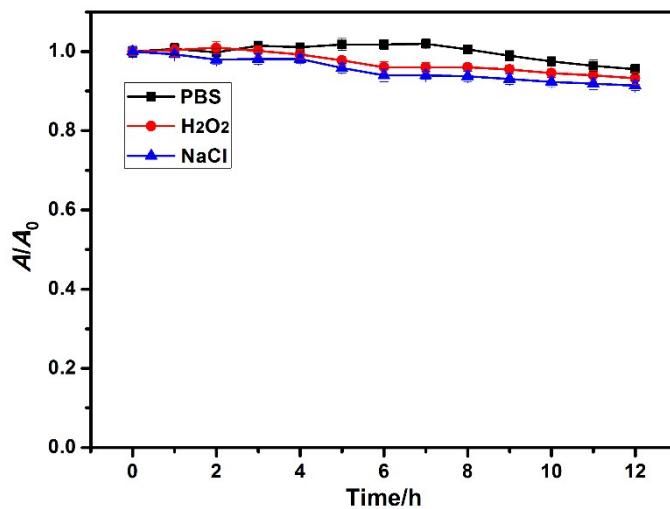
**Figure S7** UV-vis spectra (a) and Raman spectra (b) of Au@Cu<sub>3</sub>(BTC)<sub>2</sub> NPs at pH 1-8.



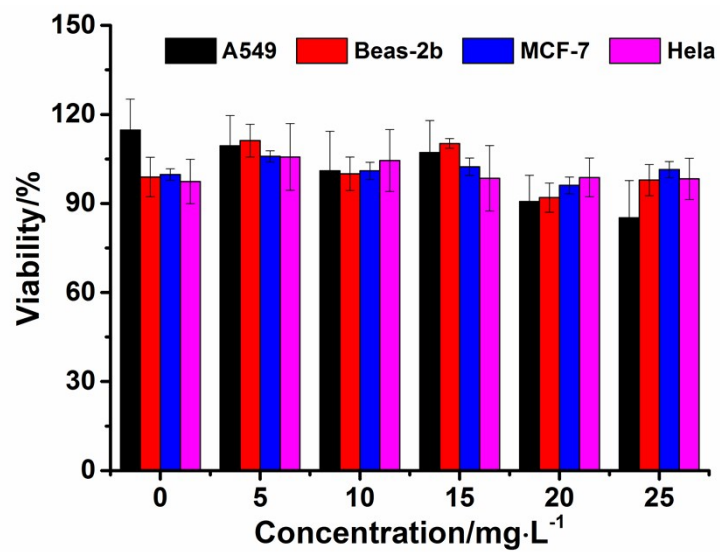
**Figure S8** (a) Raman spectra of MBA-Au NPs in the presence of different concentrations of NaCl; (b) the value of max absorbance peak (~510 nm) in UV-vis spectra of MBA-Au NPs in different concentrations of NaCl; (c) Raman spectra of Au@Cu<sub>3</sub>(BTC)<sub>2</sub> NPs labeled with MBA in the presence of different concentrations of NaCl; (d) the value of max absorbance peak in UV-vis spectra of Au@Cu<sub>3</sub>(BTC)<sub>2</sub> NPs labeled with MBA in the presence of different concentrations of NaCl.



**Figure S9** (a) Raman spectra of MBA-Au NPs in the presence of 10 mmol L<sup>-1</sup> PBS and 10 mmol L<sup>-1</sup> H<sub>2</sub>O<sub>2</sub>; (b) the value of max absorbance peak (~510 nm) in UV-vis spectra of MBA-Au NPs in the presence of 10 mmol L<sup>-1</sup> PBS and 10 mmol L<sup>-1</sup> H<sub>2</sub>O<sub>2</sub>; (c) Raman spectra of Au@Cu<sub>3</sub>(BTC)<sub>2</sub> NPs labeled with MBA in the presence of 10 mmol L<sup>-1</sup> PBS and 10 mmol L<sup>-1</sup> H<sub>2</sub>O<sub>2</sub>; (d) the value of max absorbance peak (~510 nm) in UV-vis spectra of Au@Cu<sub>3</sub>(BTC)<sub>2</sub> NPs labeled with MBA in the presence of 10 mmol L<sup>-1</sup> PBS and 10 mmol L<sup>-1</sup> H<sub>2</sub>O<sub>2</sub>.



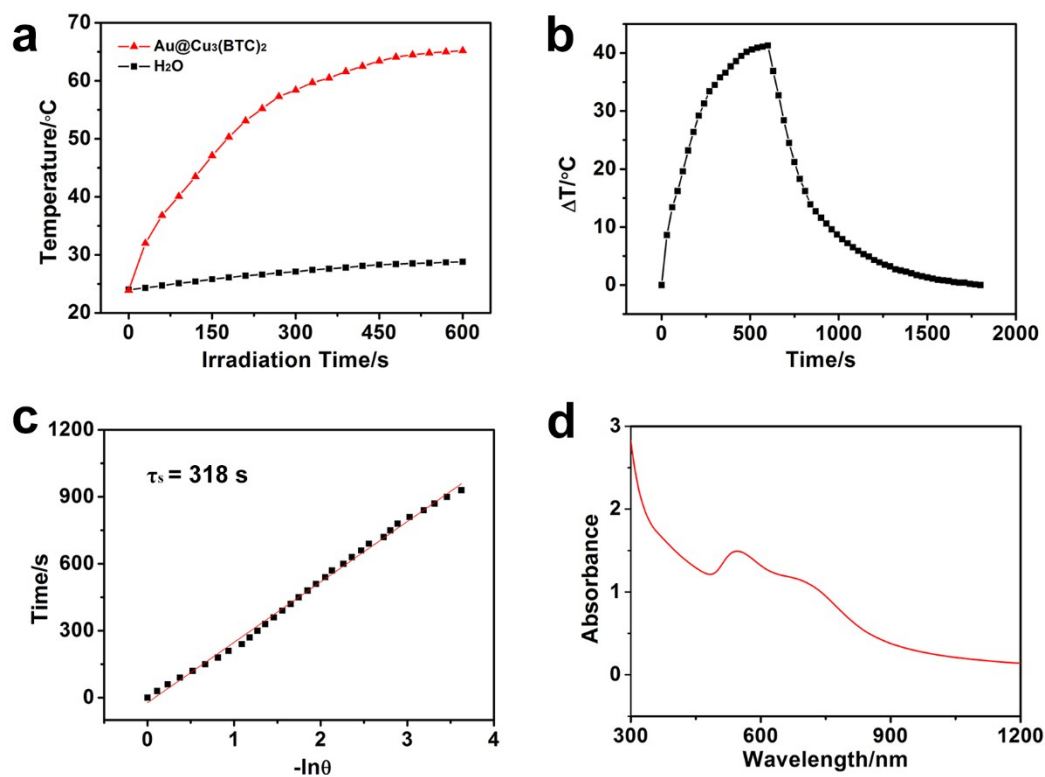
**Figure S10**  $A/A_0$  (relative absorbance intensity, where  $A_0$  and  $A$  are the optical absorbance of  $Au@Cu_3(BTC)_2$  NPs without and with the presence of  $10 \text{ mmol L}^{-1}$  PBS,  $10 \text{ mmol L}^{-1}$   $H_2O_2$ , or  $10 \text{ mmol L}^{-1}$  NaCl, respectively) at different time points.



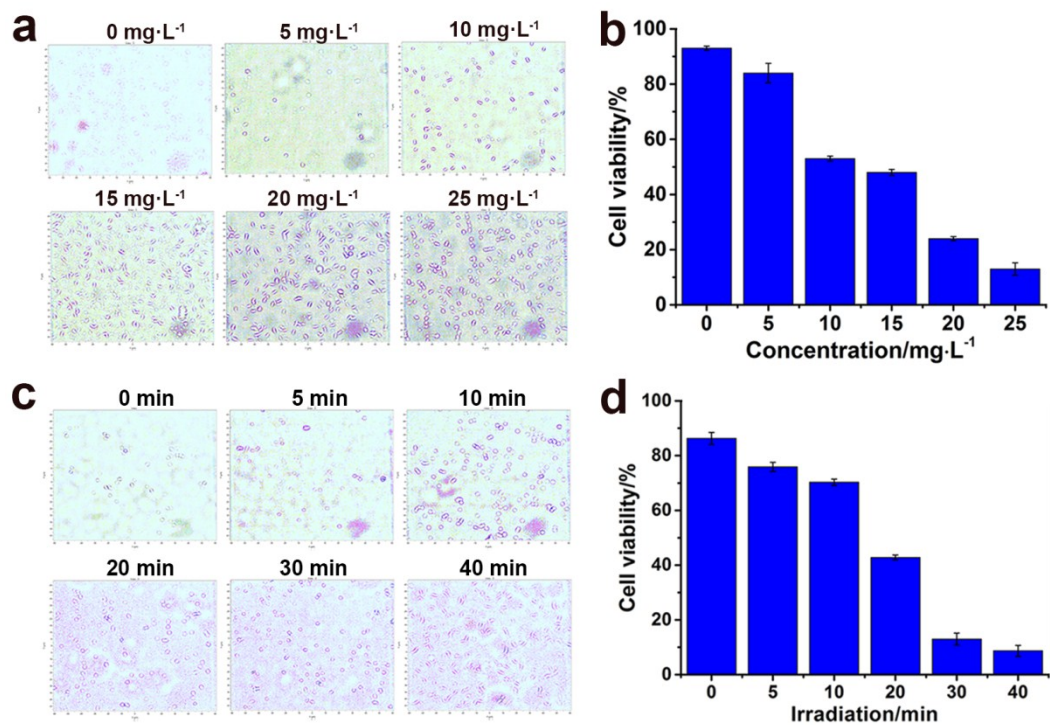
**Figure S11** Cell viability in the presence of different concentrations of Au@Cu<sub>3</sub>(BTC)<sub>2</sub>

NPs.

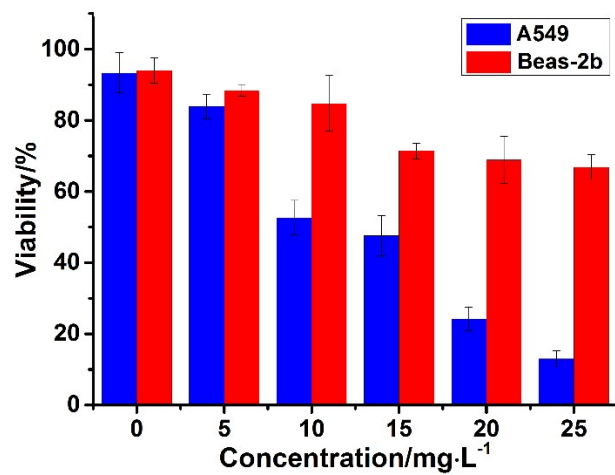




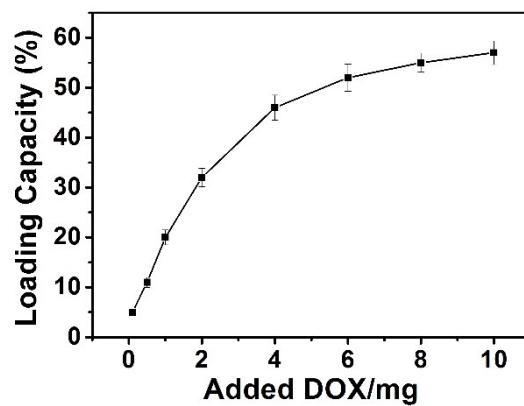
**Figure S12** (a) Temperature change curves of Au@Cu<sub>3</sub>(BTC)<sub>2</sub> and water with a continuous 600 s laser irradiation. (b) Temperature elevations of Au@Cu<sub>3</sub>(BTC)<sub>2</sub> under 600 s irradiation and subsequent cooling by terminating the irradiation. (c) Time constant ( $\tau_s$ ) is calculated to be 318 s by analyzing the linear time data from the cooling period of (b) versus negative natural logarithm of driving force temperature ( $-\ln \theta$ ). (d) Absorption spectra of Au@Cu<sub>3</sub>(BTC)<sub>2</sub> with 100  $\mu\text{g mL}^{-1}$ .



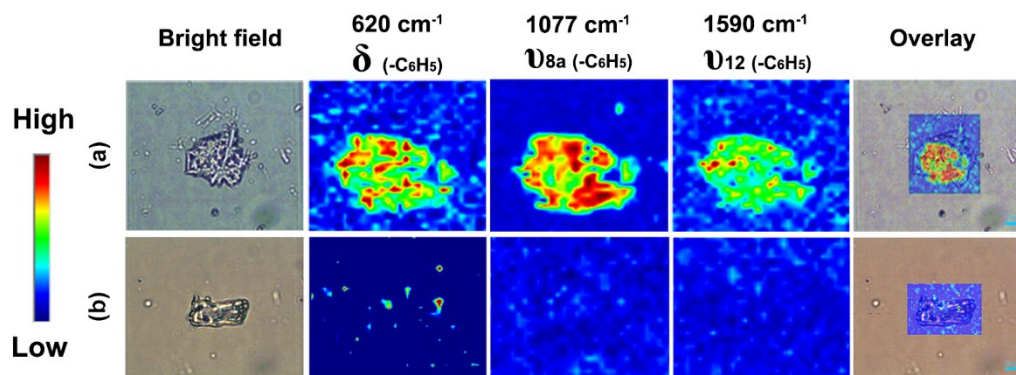
**Figure S13** Bright field microscopy images of trypan blue-stained A549 (a) and relative cell viability of A549 (b) after treatments with different concentrations of Au@Cu<sub>3</sub>(BTC)<sub>2</sub> NPs and NIR irradiation for 30 min; bright field microscopy images of trypan blue-stained A549 (c) and relative cell viability of A549 (d) after treatments with 25 mg L<sup>-1</sup> Au@Cu<sub>3</sub>(BTC)<sub>2</sub> NPs and different NIR irradiation time.



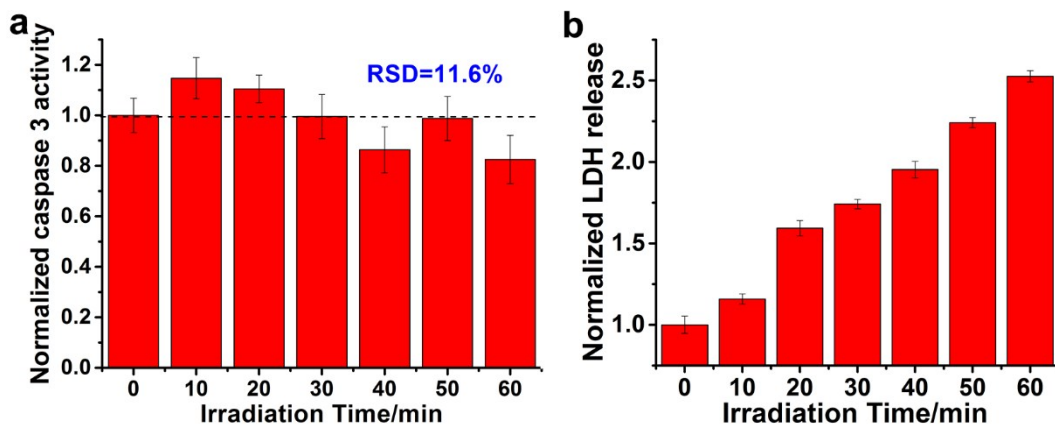
**Figure S14** Cell viability of A549 and beas-2b after treatments with different concentrations of Au@Cu<sub>3</sub>(BTC)<sub>2</sub> NPs and NIR irradiation for 30 min.



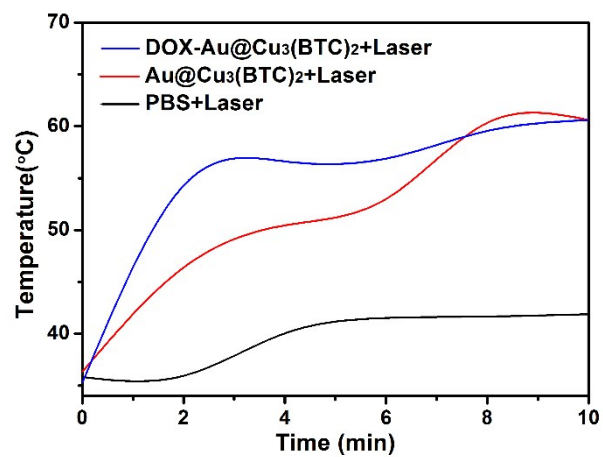
**Figure S15** Drug loading capacity of Au@Cu<sub>3</sub>(BTC)<sub>2</sub> NPs at different DOX added contents.



**Figure S16** SERS mapping of A549 treated with Au@Cu<sub>3</sub>(BTC)<sub>2</sub> modified with (a) and without aptamer. Scale bar: 10 μm.



**Figure S17** (a) Caspase 3 activity of A549 treated with different irradiation time after incubation with Au@Cu<sub>3</sub>(BTC)<sub>2</sub> NPs; (b) LDH release of A549 treated with different irradiation time after incubation with Au@Cu<sub>3</sub>(BTC)<sub>2</sub> NPs.



**Figure S18** Temperature evolution curves of the tumor region under NIR irradiation.

## References

- 1 D. K. Roper, W. Ahn and M. Hoepfner, *J. Phys. Chem. C*, 2007, **111**, 3636.