Supporting Information

In situ Fabrication of Nanoprobes for ^{19}F Magnetic Resonance Imaging and Photoacoustic Imaging Guided Tumor Therapy

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List of content

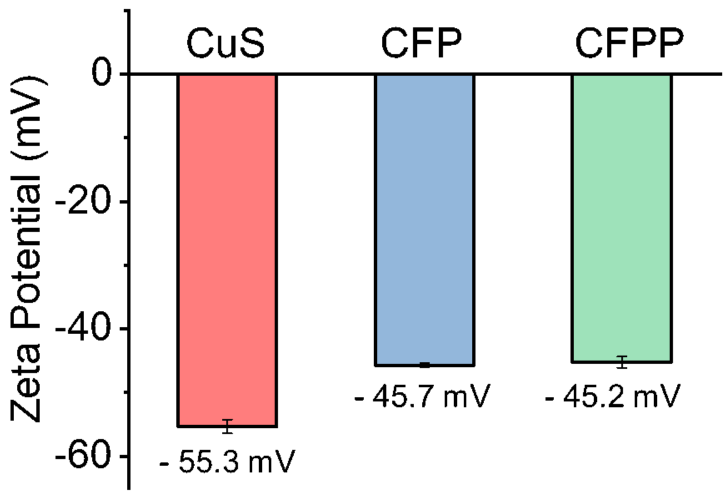

Figure S1. The zeta potential of CuS, CFP, CFPP, respectively.

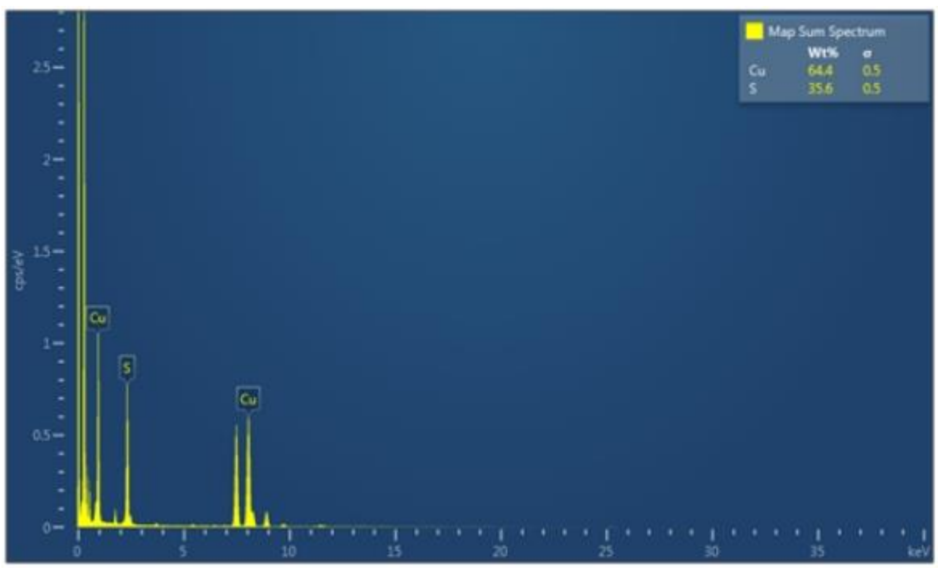

Figure S2. Energy-dispersive X-ray spectroscopy (EDS) of CFPP NPs.

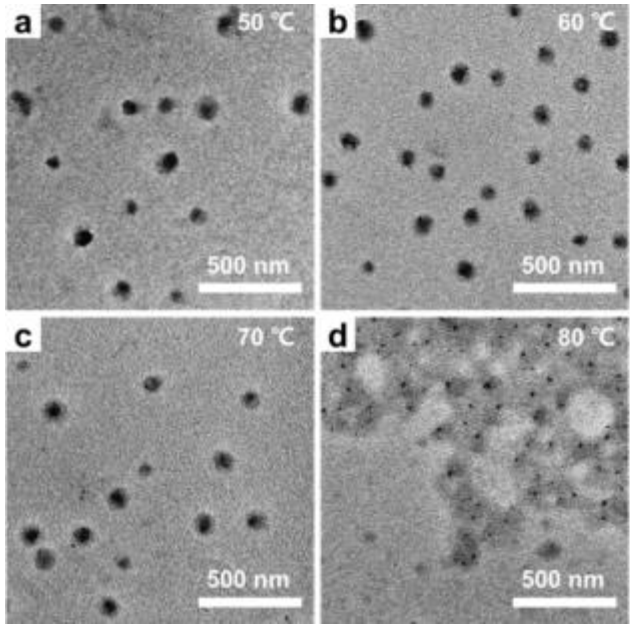

Figure S3. TEM images of CFPP NPs prepared under different temperatures (50-80°C), respectively. (a-d) represent 50°C, 60 °C , 70 °C and 80 °C, respectively.

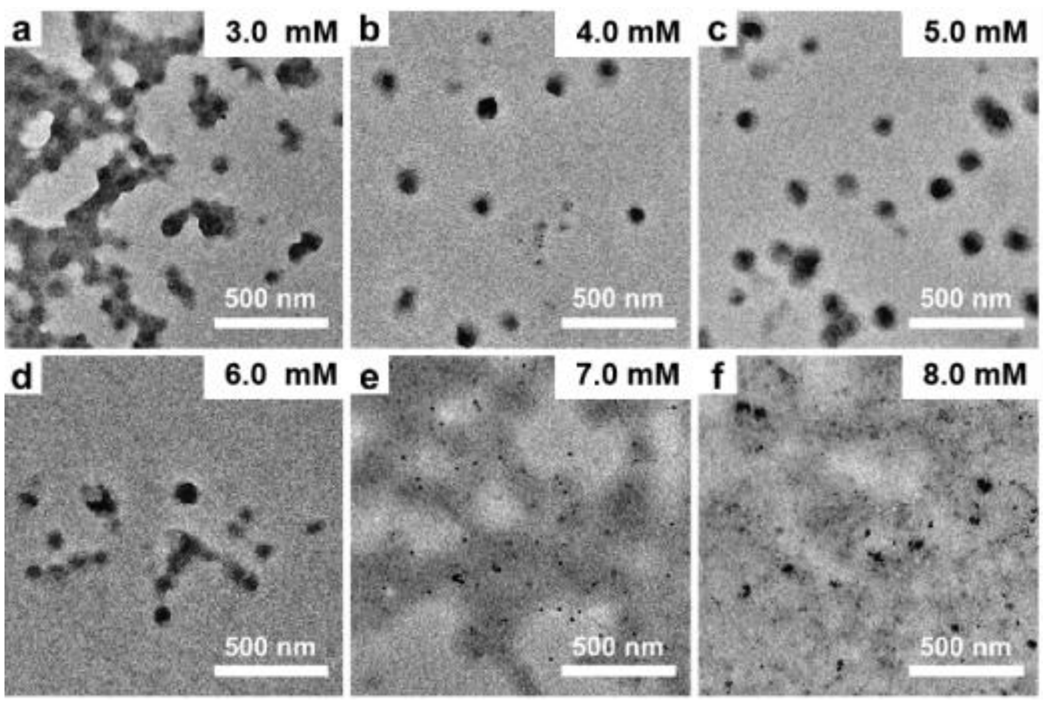

Figure S4. TEM images of CFPP NPs prepared by adding different concentrations of sodium sulphide (3.0-8.0 mM), respectively. (a-f) represent 3.0 mM, 4.0 mM, 5.0 mM, 6.0 mM, 7.0 mM and 8.0 mM, respectively.

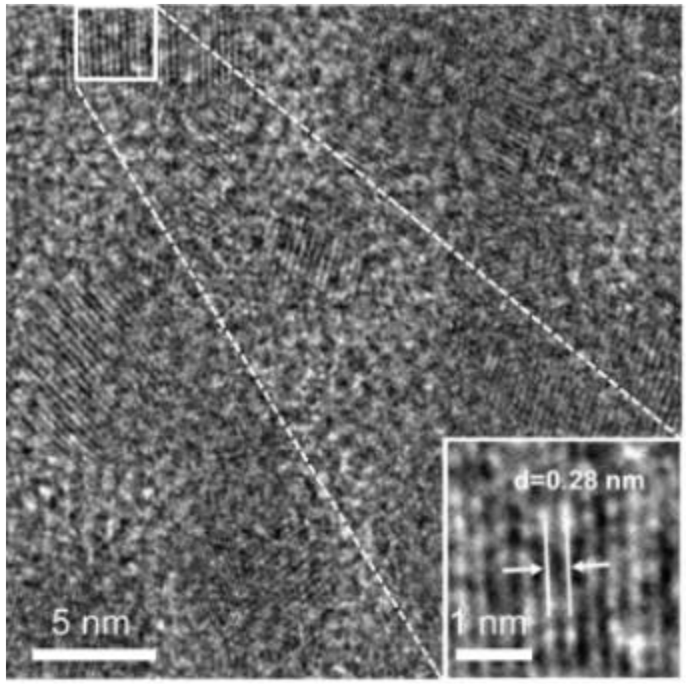

Figure S5. HRTEM image of the d-CFPP NPs. The inserted image is an enlarged area.

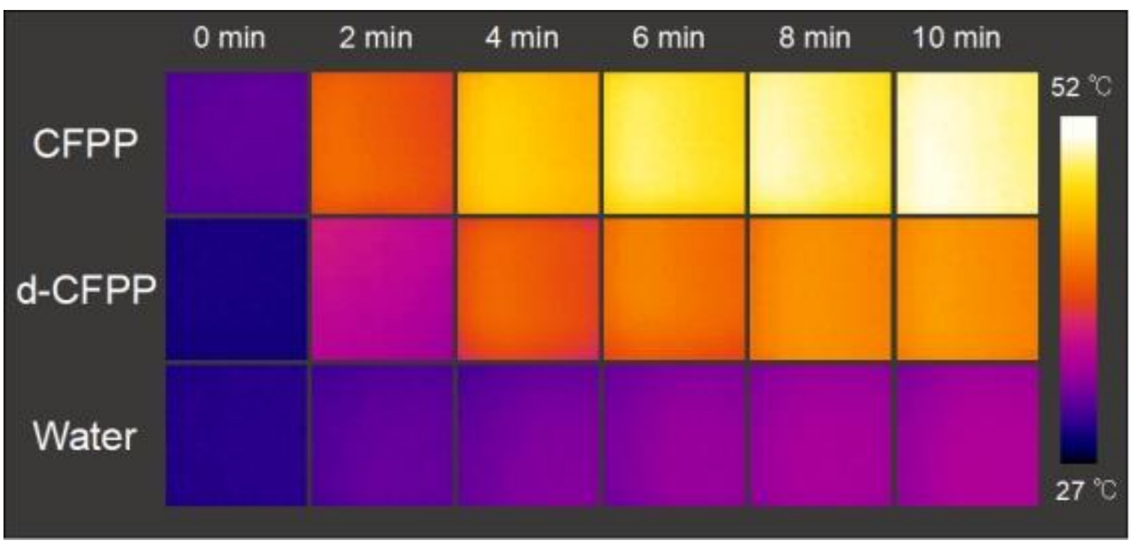

Figure S6. Photothermal images of CFPP NPs, d-CFPP NPs and water along with illumination by 1064-nm laser.

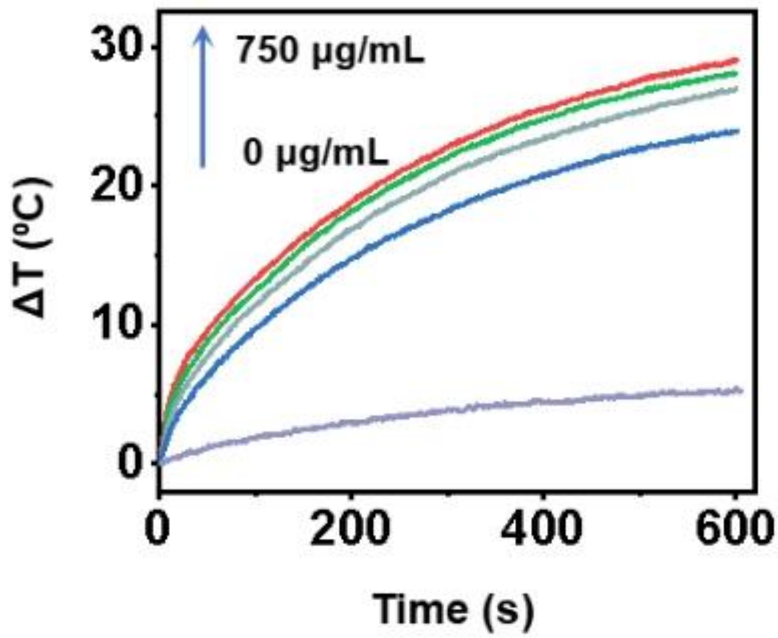

Figure S7. Photothermal performance curve of CFPP NPs with different concentrations (750 μg/mL, 500 μg/mL, 250 μg/mL, 125 μg/mL, 0 μg/mL).

Calculation of the Photothermal Conversion Efficiency:

The calculation of the photothermal conversion efficiency *(η)* is based on the previous work,[1-2] using the following series of formulas:

$$Q_{NPs} = I(1 - 10^{-A_\lambda})\eta \qquad (S1)$$

$$\sum_i m_i C_{p,i} \frac{dT}{dt} = Q_{NPs} + Q_S - Q_{loss} \qquad (S2)$$

C_p and m are the heat capacity and mass, T is the solution temperature. Q_{NPs} is the photothermal energy absorbed by nanoparticles per second, Q_s is the heat associated with the light absorbed by solvent per second and Q_{loss} is thermal energy lost to the surroundings.

$$Q_{loss} = hA \triangle T \qquad (S3)$$

I is the laser power, A_λ is the absorbance of NPs in an aqueous solution. In this system, the absorption of NPs at 1064nm was selected. h is the heat transfer coefficient, A is the surface area of the container, and ΔT is the changed temperature, which is referred to $T\text{-}T_{amb}$.

In a dispersed system of water, the heat input is equal to the heat output at the maximum steady-statue temperature:

$$Q_S = Q_{loss} = hA \triangle T_{max,\,H_2O} \qquad \text{(S4)}$$

In a dispersed system of nanoparticles, 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-statue temperature:

$$Q_{NPs} + Q_S = Q_{loss} = hA \triangle T_{max,\ mix} \qquad \text{(S5)}$$

Thus, the formula for calculating the photothermal conversion efficiency can be derived:

$$\eta = \frac{hA(\triangle T_{max,\ mix} - \triangle T_{max,\ \ H_2O})}{I(1-10^{-A_\lambda})} \qquad \text{(S6)}$$

To get the hA, we introduce θ, which is defined as the ratio of ΔT to ΔT_{max}

$$\theta = \frac{T_{amb} - T}{T_{amb} - T_{max}} \qquad \text{(S7)}$$

Substituting equation (S7) into equation (S2):

$$\frac{d\theta}{dt} = \frac{hA}{\sum_i m_i C_{p,i}}\left(\frac{Q_{NPs} + Q_s}{hA \triangle T_{max}} - \theta\right) \qquad \text{(S8)}$$

When the laser is removed,

$$Q_{NPs} + Q_S = 0 \qquad \text{(S9)}$$

$$dt = -\frac{\sum_i m_i C_{p,i}}{hA}\frac{d\theta}{\theta} \qquad (S10)$$

$$t = -\frac{\sum_i m_i C_{p,i}}{hA} ln\theta \qquad (S11)$$

τ_s can be introduced to represent $\frac{\sum_i m_i C_{p,i}}{hA}$, which means the sample system time constant. Therefore, hA can be obtained through linear fitting the graph of τ_s against $-ln\theta$. Then η can be obtained.

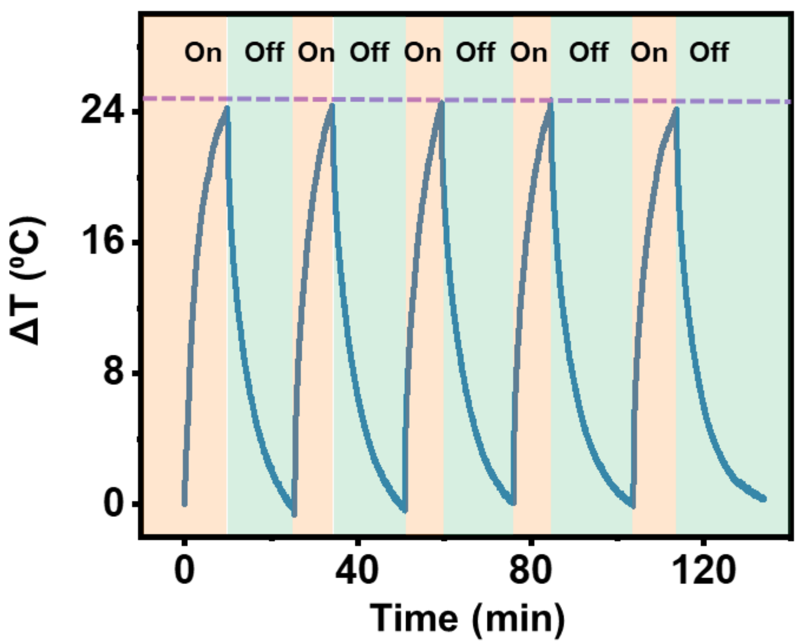

Figure S8. The photothermal effect of CFPP NPs (500 μg/mL) upon five cycles by switching the laser on/off.

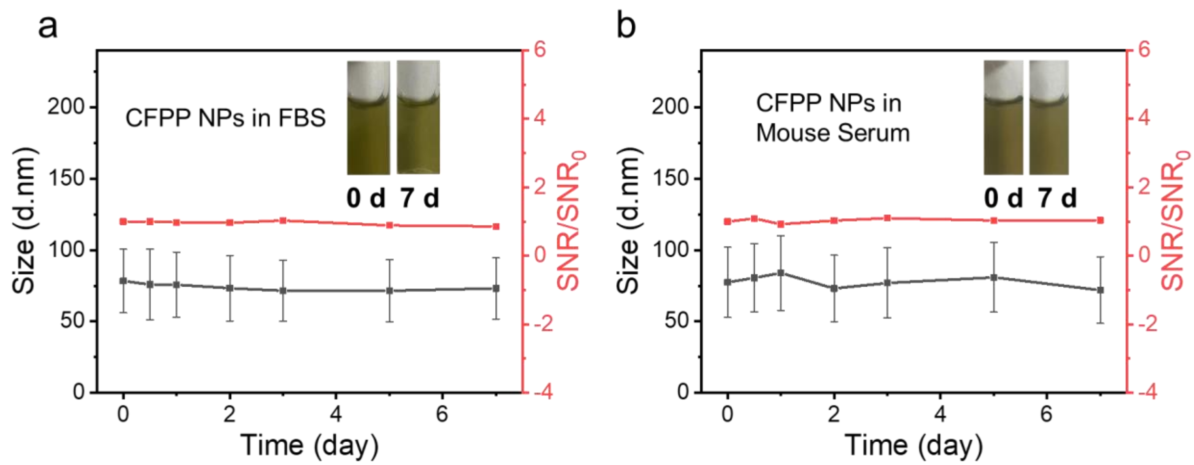

Figure S9. Size distributions and ^{19}F SNR intensity evolution of CFPP NPs after incubation in FBS (a) or Balb/C mouse blood serum (b) at 37°C for 7 days

Table S1. Stability tests of CFPP NPs

Time (day)	Chemical shift (ppm) of ^{19}F NMR	Signal-to-noise ratio (SNR) of ^{19}F NMR	Peak width at half height (Hz) of ^{19}F NMR	Dynamic light scattering (DLS) size in water (nm)	Dynamic light scattering (DLS) size in PBS (nm)
0	-91.87	8621.33	18.59	77.64 ± 20.99	72.47 ± 20.57
7	-91.89	9260.18	18.40	78.60 ± 20.66	74.18 ± 19.48
14	-91.91	8934.21	17.43	78.76 ± 20.59	70.35 ± 19.41
21	-91.90	9188.66	17.51	73.88 ± 20.08	71.49 ± 21.32
28	-91.90	8647.61	17.00	70.63 ± 19.67	70.58 ± 19.39

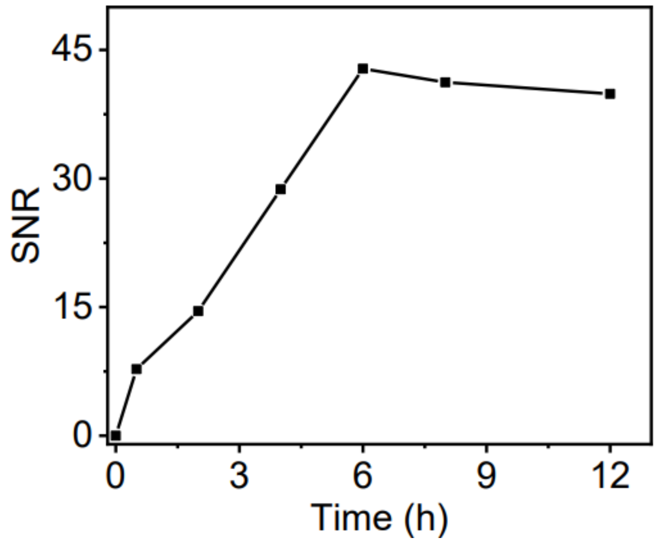

Figure S10: ^{19}F NMR spectra of 4T1 cells lysates after incubation with CFPP for different time intervals.

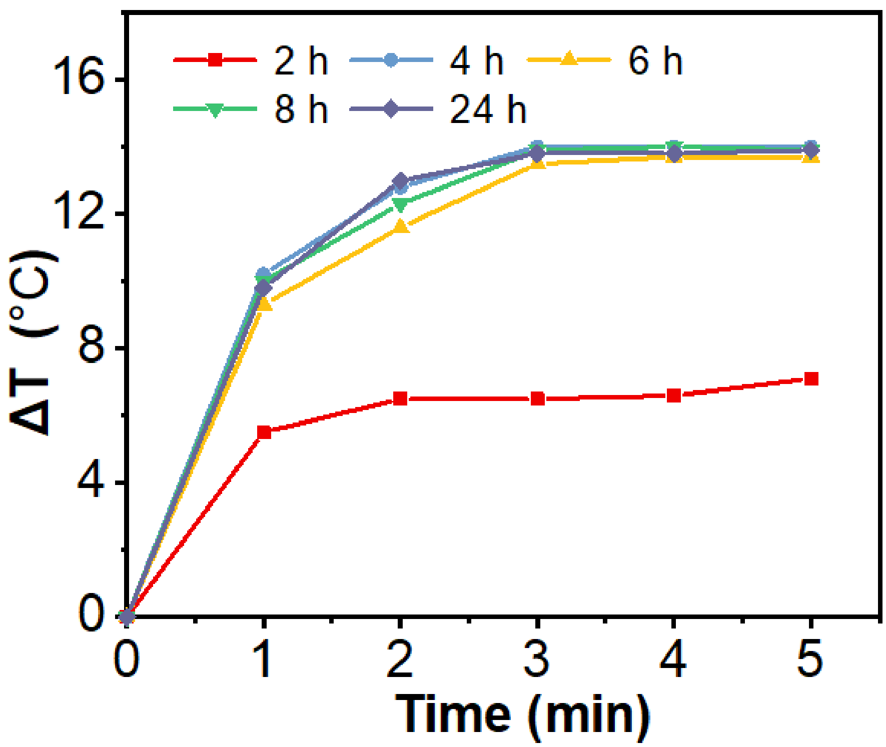

Figure S11: Temperature evolution profile of mice after injection of CFPP NPs at 2 h, 4 h, 6 h, 8 h and 24 h, respectively.

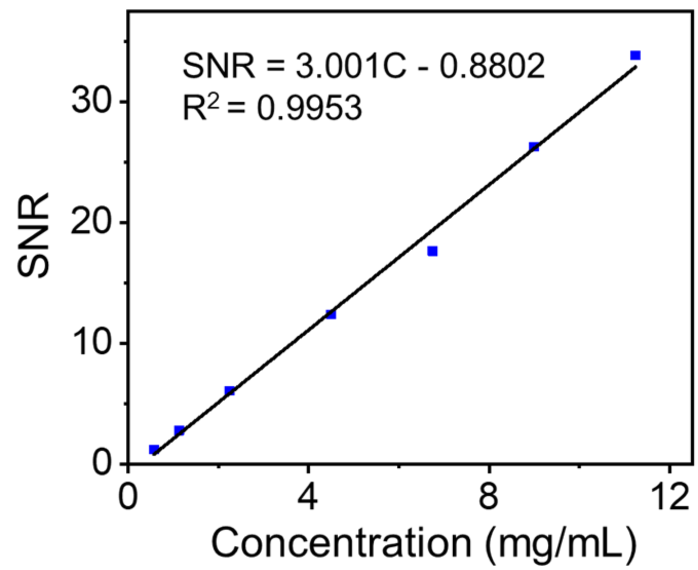

Figure S12. The plot of the ^{19}F MRI signal-to-noise ratio (SNR) *versus* CFPP NPs concentration.

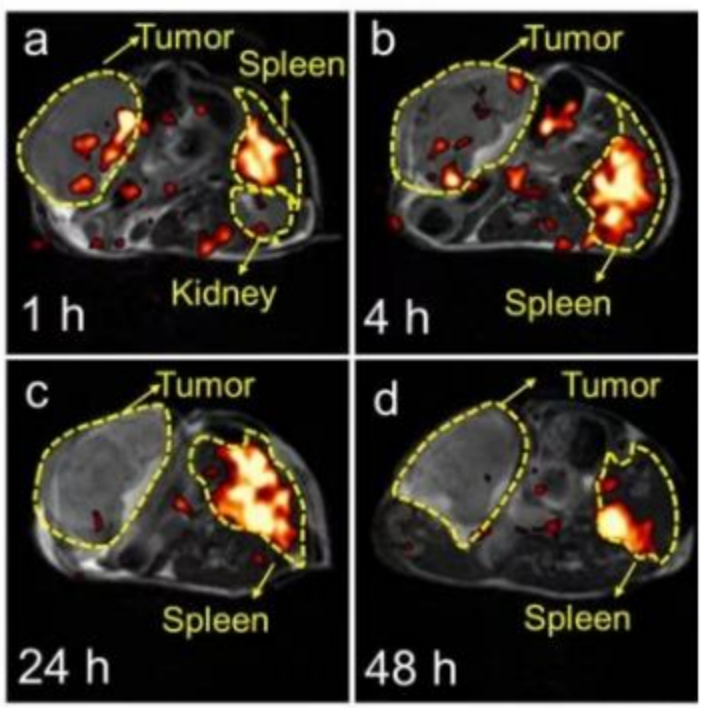

Figure S13. *In vivo* ^{1}H and ^{19}F MRI images of the tumor-bearing mice at different time intervals after intravenous injection of CFPPs (i.v.). (a-d) represent 1, 4, 24 and 48 h, respectively.

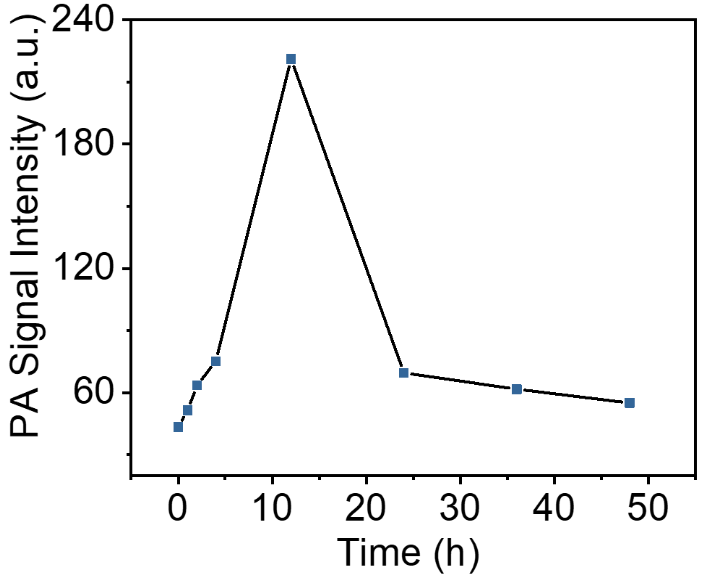

Figure S14. *In vivo* PA signals of tumor site at different time after intravenous of CFPP NPs.

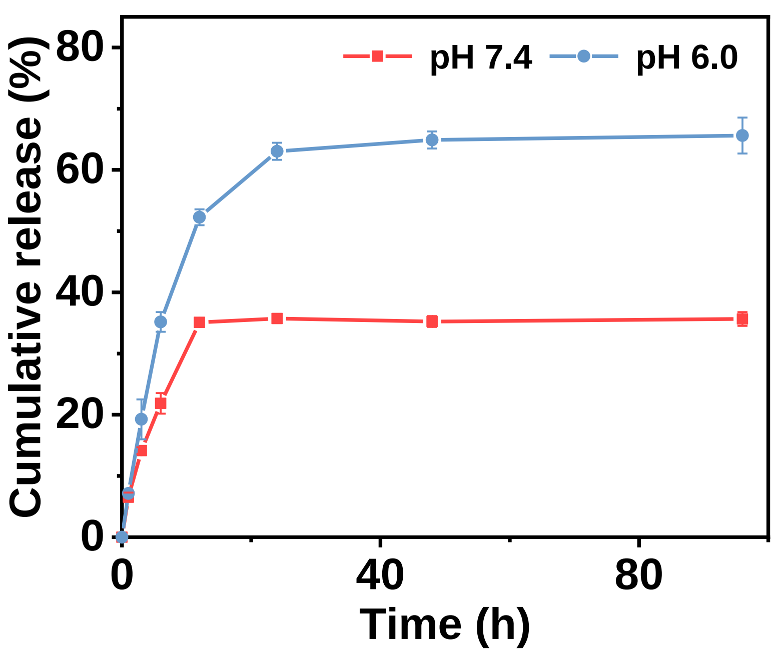

Figure S15. Release curves of PTX for CFPP NPs under different pH conditions.

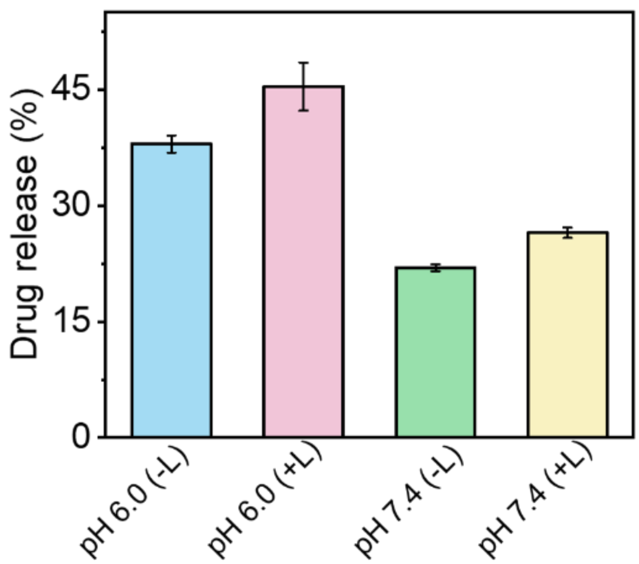

Figure S16. The release percentages of PTX for CFPP NPs under different conditions after dialysis for 6 hours.

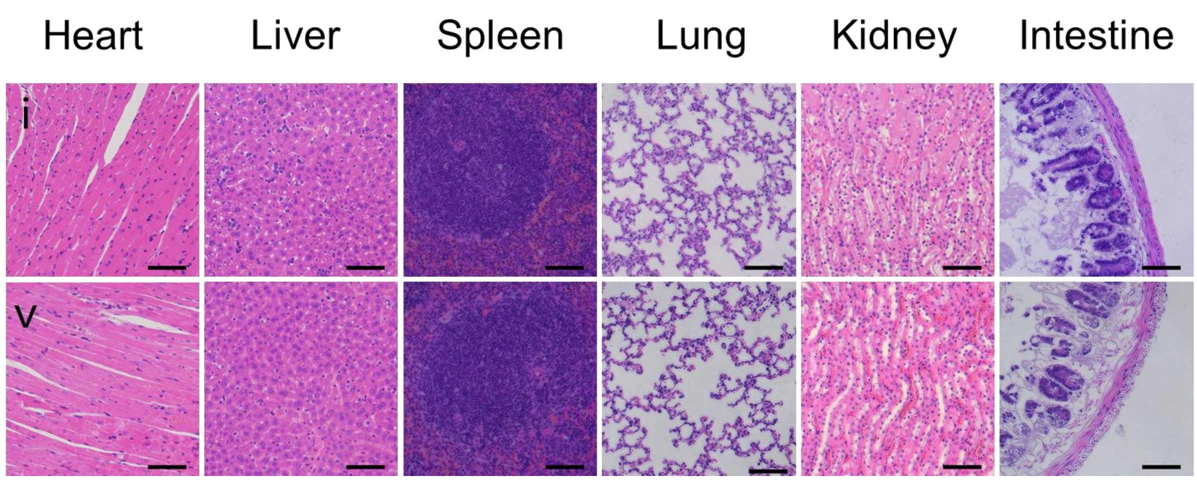

Figure S17. H&E-stained slices of different tissues from different groups. Scale bar: 50 µm. (i) PBS, (v) CFPP NPs + Laser.

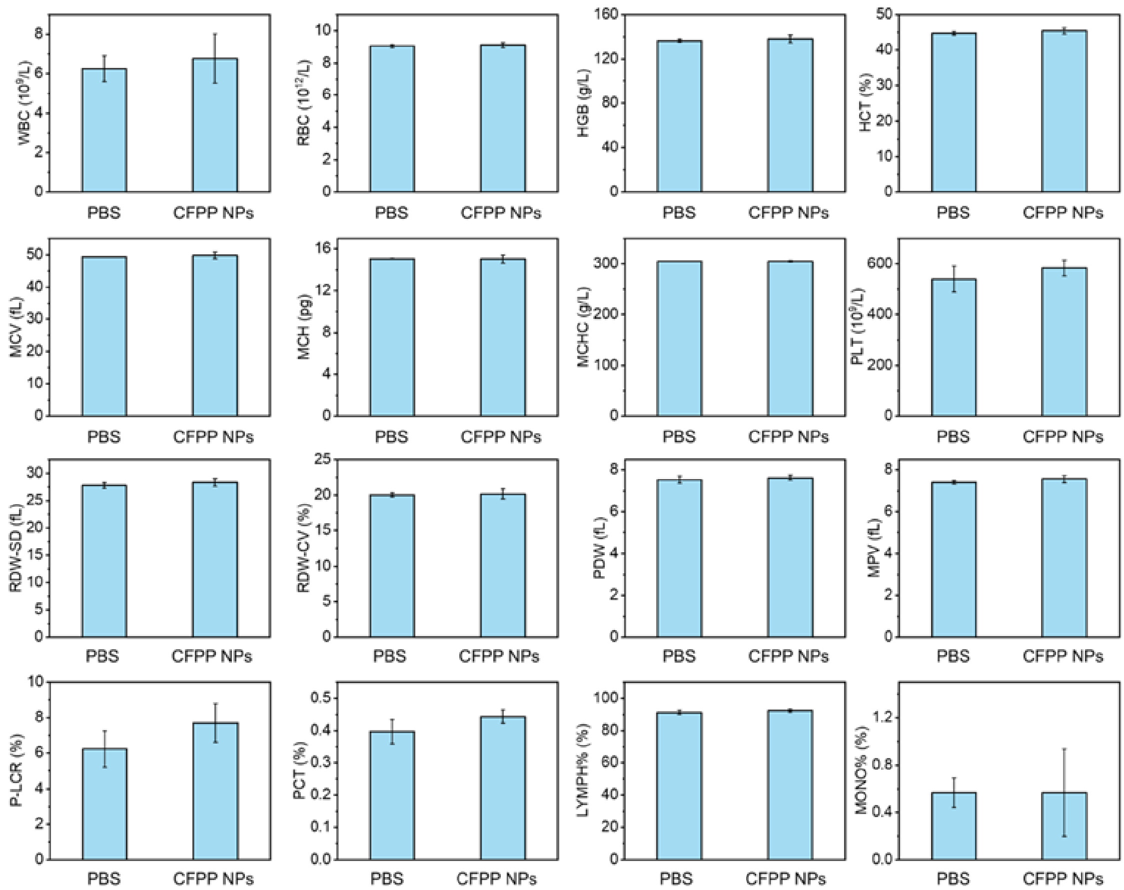

Figure S18. The mice blood biochemistry assay data. (n = 3)

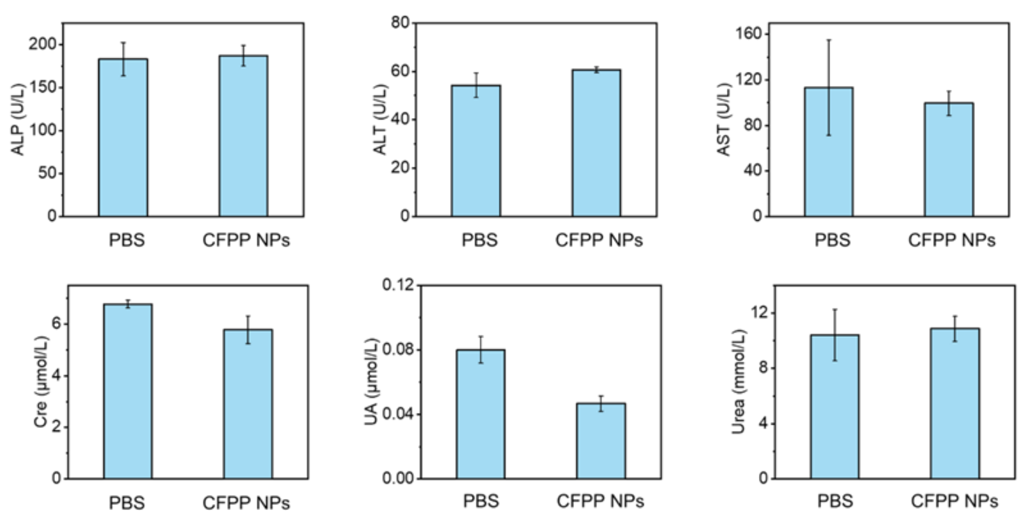

Figure S19. The mice liver and kidney function blood tests. (n = 3)

References

[1] Ren, W. Z.; Yan, Y.; Zeng, L. Y.; Shi, Z. Z.; Gong, A.; Schaaf, P.; Wang, D.; Zhao, J. S.; Zou, B. B.; Yu, H. S.; Chen, G.; Brown, E. M. B.; Wu, A. G. *Adv. Healthc. Mater.* **2015,** *4*, 1526-1536.

[2] Roper, D. K.; Ahn, W.; Hoepfner, M. *J. Phys. Chem. C* **2007,** *111*, 3636-3641.