Supplemental information

Nanoplatforms with synergistic redox cycles and rich defects for activatable image-guided tumor-specific therapy

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Supplemental Experimental Procedures

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Experimental section

Chemicals and Reagents

General chemicals were available with the highest grade and used without further purification. Analytical-grade ethanol, methanol, \( N, N \)-dimethyl formamide (DMF), dimethylsulfoxide (DMSO), cyclohexane, chloroform, NaOH were acquired from Beijing Chemical Reagent Company. Poly(succinimide) (PSI, \( M_w \approx 7000 \)) was supplied by Shijiazhuang Desai Chemical Company, China. Oleylamine (OAm, 80–90\%, Acros, USA), and 1-octadecene (ODE, 90\%, Alfa) were used. \( \text{Cu(CH}_3\text{COO)}_2\cdot4\text{H}_2\text{O} \) and \( \text{Mn(CH}_3\text{COO)}_2\cdot4\text{H}_2\text{O} \) of analytical grade were purchased from Tianjin Fuchen Chemical Reagent Company. Sulfur was obtained from Xilong Chemical Reagent Company. PFCE was supplied by Fluorochem. Ltd. Paraformaldehyde was purchased from Tianjin Chemical Reagent Company. Calcein Acetoxyethyl Ester (Calcein AM) and Propidium Iodide (PI) were purchased from Beyotime. Methylene blue (MB) was purchased from Tianjin Guangfu Chemical Reagents Company. Isoflurane was obtained from Shanghai Yuyan Instruments Co., LTD. 1,3-Diphenylisobenzofuran (DPBF) and methyl thiazolyl tetrazolium (MTT) were purchased from Sigma Aldrich. Ultrapure water was supplied by a Milli-Q water purification system from Millipore (Bedford, MA, USA). 2,7-Dichloro-hydrofluorescein diacetate (DCFH-DA) was obtained from MACKLIN. 5,5′-dithiobis (2-nitrobenzoic acid) (DTNB) and 5,5-dimethyl-1-pyrroline N-oxide (DMPO) were purchased from Shanghai Bid Pharmaceutical Technology Co., 3,3′,5,5′-Tetramethylbenzidine dihydrochloride (TMB) was purchased from Aladdin.

Characterization

Transmission electron microscopic (TEM) images were collected using a JEOL JEM-1200EX with 100 KV accelerating voltage. High-resolution transmission electron microscopic (HRTEM) images were obtained by JEM-2100 (200 KV). X-ray diffraction (XRD) patterns were recorded on a Bruker AXS D8-Advanced X-ray diffractometer with Cu K\( \alpha \) radiation (\( \lambda = 1.5418 \) Å). Dynamic light scattering (DLS) particle size analysis and zeta potential tests were carried out by a Zetasizer Nano-ZS90 zeta and size analyzer from Malvern. Electron paramagnetic resonance (EPR) spectra were obtained on a Bruker E500-10/12 Electron Paramagnetic Resonance Spectrometer. Raman spectra were obtained on a Bruker Fourier Transform
Infrared Raman spectrometer using 532-nm laser excitation. UV-vis absorption spectra were obtained on UV-3600 UV–vis–NIR spectrophotometer (Shimadzu). $^{19}$F NMR spectra were evaluated on a Bruker Avance-III 400 instrument at 376 MHz. The prepared materials were dispersed in water or phosphate-buffered saline (PBS) solution with a coaxial D$_2$O-filled capillary tube for field locking and shimming. The major parameters are as follows: the spectral width (89,286 Hz); the FID size (64 k); the acquisition time (0.367 s); the accumulation number (128); the relaxation delay (2 s); and the pulse angle (45°). The t1r pulse sequence was used to determine $T_1$, while the Car-Purcell-Meiboom-Gill (CPMG) pulse sequence was used to detect $T_2$. The elemental content was analyzed by an inductively coupled plasma optical emission spectrometer (ICP-OES, Thermo Scientific iCAP 6000 series). X-ray photoelectron spectra (XPS) were measured on an X-ray photoelectron spectrometer from Thermo Fisher Scientific USA. The cell viability test was performed on a Tecan Infinite F50 (Switzerland) plate reader. 1064-nm diode laser with a fiber optic accessory was supplied by Beijing Hi-Tech Optoelectronic Co. The output power density was independently calibrated using an optical power meter (Beijing Taught Jinyuan technology Co.). The concentration of oxygen was detected by a dissolved oxygen instrument (F4-Field portable dissolved oxygen meter, METTLER TOLEDO). Cell imaging was performed on a NIKON ECLIPSE Ti2 microscope with an excitation of 504 nm. The photothermal imaging tests were performed on a Flir A615 camera (Sweden). All of the MRI images were taken on a 7.0 T Bruker BioSpec70/20USR MRI system.

**Preparation of oleylamine-grafted polysuccinimide (PSI$_{OAm}$)**

The PSI$_{OAm}$ was synthesized according to our previous method with some modifications.$^{1-3}$ Polysuccinimide (PSI, 1.6 g) was dissolved in 32 mL DMF at 90 °C before 2.16 mL of oleylamine was added to functionalize the PSI and render it amphiphilic. The obtained solution mixture was then stirred for 5 h at 100 °C. The product was acquired by precipitation using methanol and centrifuged at a speed of 7000 rpm for 5 min after being cooled to room temperature. The final product was dispersed in chloroform for further use.

**Steady-state kinetic assays of the OXD-like activity**

The steady-state kinetic assays were conducted at 25 °C in a 0.02 M PBS (pH 6.0) with CMCF NCs (100 μg mL$^{-1}$), by adding different amounts (0, 0.025, 0.05, 0.1, 0.2, 0.3, 0.4 and
0.5 mM) of TMB (as the substrate) solution (dissolved in ethanol). The absorption of the resulting solutions were monitored at different reaction time intervals. Catalytic parameters were calculated by fitting the absorbance data to the Michaelis-Menten equation (Eq. 1).

\[ \nu = \frac{v_{\text{max}}[S]}{K_m + [S]} \quad \text{Eq. 1} \]

In this equation, \( \nu \) is the initial velocity, \( v_{\text{max}} \) is the maximum reaction velocity, \([S]\) is the concentration of substrate (TMB) and \( K_m \) is the Michaelis constant. The Michaelis constant is equivalent to the substrate concentration at which the initial velocity is half of \( v_{\text{max}} \). \( K_m \) indicates the affinity of the enzyme toward the substrate and a lower \( K_m \) value means higher affinity.

**Steady-state kinetic assays of the POD-like activity**

The steady-state kinetic assays were conducted at 25 °C in a 0.02 M PBS (pH 6.0) with CMCF (100 μg mL\(^{-1}\)) and 1 mM TMB. The kinetic assays of CMCF were determined using \( \text{H}_2\text{O}_2 \) as the substrate in the presence of 1 mM of TMB and 100 μg mL\(^{-1}\) of CMCF. A series of concentrations of \( \text{H}_2\text{O}_2 \) (0, 0.25, 0.5, 1, 2, 3, 4 and 5 mM) were used to investigate the steady-kinetic assays. The absorbance of products was monitored at different reaction time intervals. Catalytic parameters were calculated by fitting the absorbance data to the Michaelis-Menten equation (Eq. 1).

**Photothermal tests and imaging**

The temperature changes of samples with different concentrations under different power densities were recorded using an online-type thermocouple thermometer. To assess the photothermal conversion efficiency, the temperature of aqueous CMCF NCs was recorded as a function of time under continuous irradiation of the 1064-nm laser with a power density of 1.5 W cm\(^{-2}\) until the temperature reached a steady-state. The photothermal stability was measured via the same method by repeatedly switching the laser on/off.

**Photothermal conversion efficiency measurement**

According to Roper’s report,\(^4\) the photothermal conversion efficiency (\( \eta \)) was obtained by Eq. 2.

\[ \eta = \frac{hA(T_{\text{max}} - T_{\text{min}}) - Q_0}{I(1 - 10^{-\alpha d})} \quad \text{Eq. 2} \]
\[ \tau_s = \frac{m_D C_D}{hA} \quad \text{Eq. 3} \]

\[ \theta = \frac{T_{\text{amp}} - T}{T_{\text{amp}} - T_{\text{max}}} \quad \text{Eq. 4} \]

where \( h \) is the heat transfer coefficient, \( A \) is the surface area of the container, and the value of \( hA \) can be obtained from Figure S27. \( T_{\text{max}} \) is the maximum system temperature, \( T_{\text{amb}} \) is the ambient surrounding temperature, and \((T_{\text{max}} - T_{\text{amb}})\) was calculated to be 34.2 °C according to Figure S27A (4 mg mL\(^{-1}\)). \( I \) is the laser power in units of mW (1500 mW) and \( A_i \) is absorbance (0.831) at 1064-nm. The \( Q_0 \) was measured using a quartz cuvette cell containing pure water and measured to be 152 mW using an optical power densitometer. The \( hA \) was acquired by measuring the drop rate of temperature after removing the light source and the value of \( hA \) is calculated according to Eq. 3 and Eq. 4. Where \( \tau_s \) is the sample time constant, \( m_D \) and \( C_D \) are the mass (1.0 g) and heat capacity of deionized water used as solvent, respectively. Thus, the 1064-nm photothermal conversion efficiency (\( \eta_T \)) of CMCF NCs can be calculated to be 36.1%.

**Intracellular ROS imaging**

4T1 cells and MREpiC cells were seeded on a 12-well cell culture plate and cultured at 37 °C for 24 hours. Then, the as-prepared CMCF NCs solution was added into each well, respectively, with a final concentration of 150 \( \mu \)g mL\(^{-1}\). PBS with the same volume was added as the control group. Next, the cells incubated with CMCF NCs were washed 3 times with PBS. The cells were then incubated with 2',7'-dichlorodihydrofluorescein diacetate (DCFH-DA, 10 \( \mu \)M) as ROS fluorescent probe for another 30 min and washed 3 times with PBS. Finally, the ROS fluorescent signal obtained from the oxidation of DCFH-DA probe was observed by fluorescence microscope.

**Intracellular GSH depletion**

4T1 cells were seeded in a sterilized culture flask and cultured at 37 °C in a 12-well cell culture plate for 24 hours, which were divided into three groups (\( n = 4 \)). For the control group, 100 \( \mu \)L of PBS was added. Then, 100 \( \mu \)L of as-prepared CMCF NCs was added into each well with final concentration of 50 and 100 \( \mu \)g mL\(^{-1}\), respectively. The cells were incubated for another 6 h, and were then washed 3 times with PBS. Next, the cells were lysed and centrifuged.
(10,000 rpm, 10 min). The supernatant was incubated with DTNB as the GSH indicator for 10 minutes to measure the absorption spectra

**Live and dead cell viability assay**

4T1 cells were seeded on a sterilized culture flask and cultured at 37 °C in a 12-well cell culture plate for 24 hours, which were divided into three groups: 1) Control group, 2) CMCF NCs + NIR, and 3) CMCF NCs without laser. For the control group, only PBS was added. The as-prepared CMCF NCs solution was added into each well for group 2 and 3 with final concentration of 500 μg mL⁻¹. Prior to laser treatment, the cells were further incubated for another 6 h. Then, cells in group 2 were subjected to 1064-nm laser irradiation (1.5 W cm⁻²) for 6 min before incubation for another 30 min. All the cells in the three groups were washed three times with PBS, followed by staining with Calcein AM (2 μM) and PI (10 μM). After 30 min of staining, the cells were washed with PBS three times. Fluorescence images of the cells were acquired using a confocal fluorescence microscope.
Figure S1. TEM images of CMC nanoparticles with different Mn/Cu feeding ratios. (A) 5:1, (B) 10:1 and (C) 20:1.

When the Mn/Cu ratio was 5:1, clearly CuS nanodots were obtained. Whereas, with a feeding ratio of 20:1, CMC nanocrystals with large irregular morphologies emerged. Thus, CMC nanocrystal with relatively small size and identical nanoflower-like structure was chosen under a feeding ratio of 10:1.
Figure S2. TEM images of (A) CuS nanoplates and (B) MnS nanoparticles.
Figure S3. Structural characterization and elemental analysis of CMC NFs. (A) HRTEM image and (B) EDS profile.

Judging from the HRTEM of CMC NFs, scattered CuS and Cu$_2$S domains as well as MnS domains were observed (relatively lower contrast). A lattice distance of 0.240 nm is consistent with the interplanar spacing of (1 0 2) planes for Cu$_2$S. Similarly, a lattice distance of 0.282 nm corresponds to the (1 0 3) plane for CuS. The presence of MnS was revealed by a lattice distance of 0.201 nm and 0.235 nm, which could be ascribed to the interplanar spacing of (1 1 0) and (1 0 2) planes, respectively.
Figure S4. XRD pattern of CMC NFs.
Figure S5. TEM images of CMCF NCs using different amounts of PSiOAm. (A) 20, (B) 16, (C) 12 and (D) 8 mg.
Figure S6. The intensity weighted size distribution of CMCF NCs.
Figure S7. XPS analysis of CuS NPs and CMC NFs. (A) XPS spectra of S 2p in CuS NPs and CMC NFs. (B) XPS spectra of Cu 2p in CuS NPs and CMC NFs. (C) XPS spectra of Mn 2p in MnS NPs and CMC NFs.

XPS spectra of S 2p in CuS NPs was located at 162.1 eV (S 2p^{3/2}) and 163.6 eV (S 2p^{1/2}), and XPS spectra of S 2p in CMC NFs was located at 162.4 eV (S 2p^{3/2}) and 163.8 eV (S 2p^{1/2}). A slight blue shift in binding energy of S 2p was observed in CuS, in contrast to that for MnS. Such observations suggest that the binding energies of S 2p in CMC lie in between that for MnS and CuS NPs.

XPS peaks of CMC NFs and CuS NPs suggest that the Cu 2p were located at 932.5 eV (Cu 2p^{3/2}) and 952.5 eV (Cu 2p^{1/2}), respectively, with a clear shake up satellite peak, suggesting the presence of Cu^{+} and Cu^{2+} species. The ratios of Cu^{+}/Cu^{2+} were 0.71 and 0.77 for CuS NPs and CMC NFs, respectively, which implied that a slight increase of Cu^{+} in CMC NFs.

XPS spectra of Mn 2p in MnS and CMC NFs were located at 641.8 eV (Mn 2p^{3/2}) and 653.8 eV (Mn 2p^{1/2}), and the ratio of Mn^{2+}/Mn^{3+}/Mn^{4+} in CMC (0.25:0.37:0.38) was lower than that in MnS (0.30:0.41:0.30), which revealed a valence state increase of Mn in CMC NFs. The change in valence of Cu and Mn ions indicated that electron transfer may exist from Mn to Cu in CMC NFs, resulting in slight increase of Cu^{+} and decrease of Mn^{2+}. 
Figure S8. MB degradation under different conditions. (A) Absorption spectra of MB after 2 h of incubation under different conditions and (B) corresponding optical photos. 1) 10 μg mL⁻¹ MB; 2) 10 μg mL⁻¹ MB + 1 mM H₂O₂; 3) 10 μg mL⁻¹ MB + 1 mM H₂O₂ + 400 μg mL⁻¹ CMCF NCs; 4) 10 μg mL⁻¹ MB + 400 μg mL⁻¹ CMCF NCs. It is worthy of note that the absorption spectrum of MB with H₂O₂ is almost identical to that of MB without H₂O₂. The two spectra are coincident with each other.

As shown in Figure S8, obvious degradation of MB was only observed in the presence of both CMCF NCs and H₂O₂, while H₂O₂ itself would not induce any absorption change of MB. Note that incubating CMCF NCs with MB would lead to absorption decrease of MB, which may be ascribed to non-specific adsorption as well as partial oxidation of MB on CMCF NCs.
**Figure S9.** Absorption changes of MB (10 µg mL$^{-1}$) at 665 nm at different pH values in the presence of 1 mM of H$_2$O$_2$ and 400 µg mL$^{-1}$ of CMCF NCs.
Figure S10. Absorption evolution of MB (5 μg mL⁻¹) at 665 nm under different incubation conditions in the presence of 1 mM of H₂O₂. 1) 200 μg mL⁻¹ CMCF NCs; 2) 200 μg mL⁻¹ CuSF NCs; 3) 200 μg mL⁻¹ MnSF NCs; 4) 200 μg mL⁻¹ CuSF NCs + 200 μg mL⁻¹ MnSF NCs.
Figure S11. Steady-state kinetic assay of the CMCF NCs (100 μg mL⁻¹) using H₂O₂ as the substrate and TMB as the indicator at pH 6.0. The kinetic parameters were obtained and given in the figure.
Figure S12. Optical photos of H$_2$O$_2$ solutions (100 mM) before and after adding 400 μg mL$^{-1}$ of CMCF NCs. It is clear, in the presence of CMCF NCs, large amounts of O$_2$ bubbles were observed due to the catalase (CAT)-like ability of CMCF NCs.
Figure S13. Oxidation profiles of TMB treated with CMCF NCs. (A) Absorption evolution of TMB (40 μg mL\(^{-1}\)) after being treated with 50 μg mL\(^{-1}\) of CMCF NCs at pH 6.0. (B) Time-dependent absorption of TMB (40 μg mL\(^{-1}\)) at 650 nm under different pH conditions.

We used TMB as the indicator for OXD-like activity test (Figure S13) and TMB can be oxidized into blue oxidized products in 10 min. This OXD-like activity in CMCF NCs was enhanced by weak acidic conditions, indicating the OXD-like activity can be enhanced in tumor microenvironments.
Figure S14. DPBF degradation after being treated with CMCF NCs. (A) Time-dependent absorption of DPBF (25 μg mL⁻¹) in the presence of CMCF NCs (50 μg mL⁻¹) at pH 6.0. (B) Time-dependent DPBF absorption at 420 nm at different pH values.

Besides, we also used DPBF as the probe for ·O₂⁻ (Figure S14) and DPBF can be degraded into colorless products by ·O₂⁻ quickly. Similarly, the capacity for generating ·O₂⁻ can be enhanced in weakly acidic environments.
Figure S15. Steady-state kinetic assay of CMCF as OXD-like enzyme using TMB as the substrate at pH 6.0. The kinetic parameters are given in the figure. [CMCF] = 100 μg mL⁻¹.
**Figure S16.** GSH depletion and ROS generation ability of CMCF NCs. (A) GSH depletion ability of CMCF NCs under different pH conditions by monitoring absorption changes of DTNB. (B) Absorption spectra of 4T1 cell lysate after incubation with different concentrations of CMCF NCs. (C) ROS imaging of 4T1 and MREpiC cells treated with CMCF NCs. The amount of ROS in different cell lines was monitored by ROS indicator (DCFH-DA). (D) Cell viability of 4T1 and MREpiC cells treated with CMCF NCs. Herein, 4T1 and MREpiC cells were chosen to explore cell viability due to their differences in H$_2$O$_2$ concentration and acid environment.

It is recognized that GSH could cause the degradation of DTNB, resulting in a decrease of absorption at 412 nm and the amount of GSH was proportional to the absorption of DTNB. As indicated in **Figure 16A**, under identical conditions, the absorption of DTNB decreased most significantly at pH 6.0, implying that CMCF NCs possessed the best GSH depletion capability under acidic conditions. In addition, by incubating 4T1 cells with different concentrations of CMCF NCs, it was found that less GSH was observed with an increase of CMCF NCs (**Figure 16B**), again verifying the GSH depletion ability. The amount of ROS in different cell lines was
monitored by ROS indicator (DCFH-DA). Confocal imaging of 4T1 cells showed obvious green fluorescence in Figure S16C, indicating the ROS generation in 4T1 cells. Cell viability test results suggested CMCF NCs display dramatic cytotoxicity toward 4T1 cells due to the relatively high H₂O₂ content and slightly acidic condition in 4T1 cells. Whereas there was no obvious cytotoxicity for MREpic cells even at a concentration of 225 μg mL⁻¹ (CMCF NCs) after being incubated for 48 h (Figure 16D).
Figure S17. $^{19}$F MR signal intensity of CMCF NCs at different pH values without GSH.
Figure S18. $^{19}$F NMR spectra intensity evolution versus GSH concentration under different pH conditions.
Figure S19. $^{19}$F NMR spectra evolution versus incubation time at different pH values in the presence of GSH (10 mM).
Figure S20. Optimization of the CMC dosage and the selectivity of as-prepared CMCF NCs toward various species. (A) $^{19}$F NMR signal intensities of CMCF NCs versus the dosage of CMC NFs (0.45, 0.9, 1.35, 1.8, 2.25 and 2.7 mg in 1.0 mL chloroform during the nanoplatform fabrication by ultrasonic emulsification. The red point plot is the relative intensity of $S/S_0$, where $S$ and $S_0$ represent the $^{19}$F signal intensity after and before exposure to GSH/H$^+$, respectively. $C_{\text{GSH}} = 10$ mM, pH 6.0; (B) $^{19}$F MR signal intensities towards various interference at pH 6.0. The concentration of bovine serum albumin (BSA) was 1.0 mg mL$^{-1}$, the concentration of other interferences was 10 mM. Gly, Fru, and Cys refer to glycine, fructose, and cysteine, respectively.

To obtain optimal recovery of $^{19}$F signal intensity, we first explored the dosage effect of CMC NFs (Figure S20A). The quenching degree towards $^{19}$F NMR signal continuously enhanced with an increase of CMC NFs, while once exposed to GSH/H$^+$ conditions (10 mM of GSH, pH 6.0), the $^{19}$F NMR signal displayed a dramatic increase. Reaching maximal recovery efficiency of around 3.5 (ratio of $S$ to $S_0$, where $S$ and $S_0$ represent the $^{19}$F signal intensity after and before exposure to GSH/H$^+$, respectively) when using 1.8 mg of CMC NFs (1 mL of CHCl$_3$) during the nanoplatform fabrication via ultrasonic emulsification. Thus, 1.8 mg of CMC NFs was used for preparing a TME-activable $^{19}$F MRI nanoplatform. Moreover, we also investigated the selectivity of CMCF NCs towards GSH over other potential interferents at pH 6.0 (Figure S20B). Encouragingly, CMCF NCs exhibited high selectivity towards GSH compared to other interferents, which indicated the CMCF NCs can respond to H$^+/\text{GSH}$ conditions specifically.
Figure S21. TEM images of CMCF NCs incubated with and without 10 mM GSH at different pH values for 1 h.

The TEM images in Figure S21 directly proved the GSH/H⁺ doubly triggered $^{19}$F NMR signal recovery. At pH 6.5 and 6.0, CMCF NCs can break into smaller fragments after incubation with GSH for 1 h, whereas CMCF NCs incubated with GSH at pH 7.4 exhibited relatively small changes in size and morphology, indicating that an acidic environment can accelerate the destruction of CMCF NCs under GSH-rich conditions. The result was verified mutually with size variation in DLS tests and the increase of Mn ions of the supernatant using ICP-OES tests.
Figure S22. Relaxation time measurement. (A) Transverse relaxation time ($T_2$) and (B) longitudinal relaxation time ($T_1$) change of water protons for CMCF solution (3 mg/mL) under different concentrations of GSH at pH 6.0. Insets are the corresponding $^1$H MRI images.

The variation in relaxation time towards protons for CMCF incubated with different concentrations of GSH at pH 6.0 was also investigated, as shown in Figure S22, along with an increase of GSH, the $T_2$ decreases more remarkably than that of $T_1$ relaxation time, indicating that the Mn$^{2+}$ ions released from the CMCF NCs have a greater impact on $T_2$ relaxation time of water protons. Moreover, with respect to $T_1$-weighted $^1$H MRI, the CMCF NCs displayed a $T_1$-enhanced effect, yet the released Mn species led to slightly darker image contrast in the $T_1$-weighted $^1$H MRI (Figure S22B).
Figure S23. The $T_2$-weighted $^1$H MRI images of the as-prepared CMCF nanoprobes mixed with GSH at various concentrations (0, 2, 4, 6, 8 and 10 mM).
Figure S24. Stability of CMCF NCs. (A) $^{19}$F MR signal intensity changes and (B) DLS size variation versus time, respectively. $S_0$ and $S$ refer to $^{19}$F MR signal intensity of the sample solution (pH 7.4, without GSH) freshly prepared and kept for 14 days, respectively. At day 15, $^{19}$F MR signal intensity and DLS size under TME mimicking environment (by adding 10 mM of GSH at pH 6.0) were also recorded.
Figure S25. Evaluation of photothermal properties. Photothermal curves of CMCF NCs under (A) different laser power densities with fixed amount of CMCF at 4 mg mL$^{-1}$ and (B) various CMCF NCs concentrations at a power density of 1.5 W cm$^{-2}$.

After continuous irradiation for 300 s with different laser power density, the temperature of CMCF NCs solution (4 mg mL$^{-1}$ increased to 21 °C (1.0 W cm$^{-2}$), 32 °C (1.5 W cm$^{-2}$) and 45 °C (2.0 W cm$^{-2}$), respectively. Similarly, the concentration of CMCF NCs influenced the temperature, where the temperature increased by 25.8 °C (2 mg mL$^{-1}$), 30.5 °C (4 mg mL$^{-1}$) and 37.6 °C (6 mg mL$^{-1}$), respectively, after 300 s irradiation (Figure S25B). The temperature changes were visualized using thermal imaging (Figure S26).
Figure S26. Photothermal images of CMCF NCs colloidal solution with different concentrations at different times.
Figure S27. Photothermal conversion measurements. (A) Photothermal conversion profile of CMCF NCs (4 mg mL⁻¹) under 1064-nm irradiation with power density of 1.5 W cm⁻². (B) Time constant for heat transfer of CMCF NCs. The photothermal conversion efficiency ($\eta$) of CMCF NCs was 36.1%.
Figure S28. The absorbance spectra of CMCF (4 mg mL\(^{-1}\)) before and after treatment with 10 mM GSH.
Figure S29. H&E staining of heart, liver, spleen, lung, kidney and intestine (from left to right) in groups treated by PBS and CMCF NCs with laser irradiation, respectively.
Figure S30. Blood biochemical and hematological analysis for evaluating the biosafety of different treatments. Whole blood of mice from different groups at 15 days post-injection were obtained and used for analysis: (1) PBS; (2) PBS + NIR; (3) CMCF NCs; (4) CMCF NCs + NIR. ALT, alanine transferase; AST, aspartate transferase; UA, uric acid; BUN, blood urea nitrogen; TP, total protein; ALB, albumin; GLB, globulin; RBC, red blood cells; HGB, hemoglobin; MCV, mean capsular volume; MCH, mean capsular hemoglobin; PLT, platelets.
Figure S31. Photographs of mice in groups treated with PBS + NIR light and CMCF NCs + NIR light at the 15\textsuperscript{th} day.

The treatment of CMCF NCs plus laser can ablate tumor remarkably compared with PBS plus laser, which indicates CMCF NCs effectively accumulate at the tumor site to achieve chemodynamic and photothermal synergetic therapeutic effects.
Table S1. $^{19}$F NMR properties of CMCF NCs with and without GSH at different pH values.

| Materials   | pH | GSH/mM | Half peak width/Hz | $^{19}$F NMR SNR | Chemical shift/ppm |
|-------------|----|--------|--------------------|------------------|--------------------|
| CMCF NCs    | 6.0| 0      | 43.62              | 2318             | -91.834            |
| CMCF NCs    | 6.5| 0      | 39.91              | 2254.3           | -91.855            |
| CMCF NCs    | 7.4| 0      | 43.56              | 2266.1           | -91.868            |
| CMCF NCs    | 10 | 0      | 43.56              | 2266.1           | -91.874            |
| CMCF NCs    | 10 | 10     | 24.04              | 4338.2           | -91.819            |
**Table S2.** NMR properties of CMCF, CuSF and MnSF nanocomposites with and without GSH.

| Materials  | pH | GSH/mM | T$_2$/ ms | $^{19}$F NMR SNR |
|------------|----|--------|-----------|------------------|
| CMCF       | 6.0| 0      | 23.48     | 2318             |
|            |    | 10     | 87.7      | 8126.6           |
| CuSF       | 6.0| 0      | 342.1     | 8872.3           |
|            |    | 10     | 354.8     | 9706.6           |
| MnSF       | 6.0| 0      | 13.3      | 853.8            |
|            |    | 10     | 49.1      | 3636.1           |
| PFCE@PSIOAm$^a$ | 6.0 | 0    | 352.7     | 9971.8           |

$^a$ PFCE@PSIOAm refers to PFCE encapsulated by PSIOAm without doping nanoparticles.
Table S3. Average $^{19}$F MRI SNR of different tissue areas including tumor site in liver (LIT), liver issue outside tumor (LOT) and the background.

|        | LIT  | LOT  | background | LIT/LOT | LIT/Background |
|--------|------|------|------------|---------|----------------|
|        | 9.89 | 5.09 | 2.76       | 1.94    | 3.58           |
**Table S4.** Tumor inhibition rates* of different groups

| Treatment               | Tumor inhibition rate / % |
|-------------------------|---------------------------|
| PBS + NIR               | 30.5 ± 14.4               |
| CMCF NCs                | 60.4 ± 13.7               |
| CMCF NCs + NIR          | 88.6 ± 6.8                |

* Tumor inhibition rates = 1-M/M₀*100%, M is the average mass of tumor in groups treated by PBS + NIR, CMCF NCs and CMCF NCs + NIR, M₀ is the average mass of tumor in PBS group. Data are shown as mean values ± standard deviations (n = 6)
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