Supplementary Information

Reagents and Materials.

Iron (III) chloride hexahydrate ($FeCl_3 \cdot 6H_2O$), $NaBH_4$, dimethylsulfoxide (DMSO) and ethanol were purchased from Sinopharm Chemical Reagent Co., Ltd. (China). 2-Aminoterephthalic Acid was purchased from Adamas Biochemical Technology Co., Ltd. (China). Gambogic acid (GA) and $HAuCl_4$ were purchased from Shanghai Aladdin Biochemical Technology Co., Ltd. (China). 1,3-Diphenylisobenzofuran (DPBF) was purchased from TCI (Shanghai) Development Co., Ltd. 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) was purchased from Sigma Chemical Company. Annexin V-Alexa Fluor 488/PI Apoptosis Detection Kit was purchased from Yeasen (Shanghai, China). The mouse breast cancer cell line (4T1) was purchased from Shanghai AOLU Biological Technology Co., Ltd. (China). Fetal bovine serum (FBS) in cell culture medium was purchased from Gibco. Confocal dishes were purchased from Cellvis, Mountain View, CA. All aqueous solutions were prepared using sartorius ultrapure water (18.2 $M\Omega \cdot cm^{-1}$). All chemicals were of analytical grade and were used without further purification.

Instruments. Transmission electron microscopy (TEM, HT7700, Japan) was used to characterize the morphology of the nanoparticles. The Zeta potential was recorded on a Malvern Zeta Sizer Nano (Malvern Instruments). Fluorescence spectra were obtained on a FLS-980 Edinburgh. The UV-Vis absorption spectra were measured with UV-1700 (Shimadzu, Japan). FT-IR spectra were obtained using Fourier infrared spectrometer (Nicolet iS50 FT-IR). Confocal fluorescence imaging assays were performed by a TCS SP8 confocal laser scanning microscope (Leica, Germany). In vivo fluorescence imaging experiments were tested using Bioluminescent Living Imager (IVIS Lumina III, USA). MTT assay was determined by a microplate reader (Synergy 2, Biotek, USA). All pH measurements were performed with a pH3c digital pH meter (Shanghai LeiCi Device Works, Shanghai, China) equipped with a combined glass-calomel electrode. The sections were observed through a Nikon Eclipse 80i microscope.

X-ray photoelectric spectroscopy (XPS) was measured by American Thermoelectric Thermo ESCALAB 250XI.

Preparation of MOF NPs.

2-aminoterephthalic acid was mixed with the ethanol solution containing $FeCl_3 \cdot 6H_2O$ (13.5 mg). Then water (200 μL) was added to the mixed solution and stirred at room temperature for 5 minutes. The react system was transferred to water bath (50 °C) for 1 h. Finally, the obtained MOF NPs were centrifuged and washed with water for three times.

Preparation of Au-MOF NPs.

$HAuCl_4$ and MOF nanoparticles (2 mg/mL, 1 mL) were evenly stirred in 10 mL water. Then cold $NaBH_4$ (80 μg/mL, 1 mL) was added to the above solution drop by drop under drastic agitation to generate Au-MOF NPs. The solution was centrifuged and washed with water for three times.

Preparation of Au-MOF@GA NPs.

GA (2 mg/mL, 0.5 mL) was mixed with Au-MOF (2 mg/mL, 0.5 mL) and stirred at room temperature for 12 h. The Au-MOF@GA NPs were collected by centrifugation and washed with water for three times.

Preparation of Au-MOF@GA@HA (AMGH) NPs.

EDC (10 mg) and NHS (10 mg) were added to the pH=6.5 MES solution of HA (10 mg) and kept in dark place for 0.5 h. The Au-MOF@GA (1 mg) was added in the above-mentioned solution for 6 hours. Then the Au-MOF@GA@HA nanoparticles were collected via centrifugation (13000 rpm, 10 min) and washed with water for subsequent use.

UV-Vis absorbance curves of GA.

GA solutions with a concentration gradient from 10-80 μg/mL were prepared, and the absorbance spectra from 300-800 nm were recorded.

Evaluation of the photothermal performance of MOF and Au-MOF.

To evaluate the photothermal conversion performance of MOF and Au-MOF, MOF or Au-MOF solution in the quartz cuvette was irradiated with 635 nm laser (0.5 W/cm^2) for 600s and the temperature was recorded every 20 seconds.

GSH-triggered MOF structure collapse.

MOF (1.0 mg/mL) was dispersed in water with or without GSH (10 mM) for 24 h. The morphology of nanomaterials was characterized by TEM.

The GOx-like activity of Au-MOF.

Glucose (1 mg/mL) was mixed with MOF/Au-MOF solution. The pH of the solutions was monitored over time using a pH meter.

The consumption of GSH by MOF.

GSH (10 mM) was incubated with MOF of different concentrations (0, 100, 200, 300, 400 ug/mL) for 24 h. The solution was centrifuged and DTNB (5,5'-Dithiobis-(2-nitrobenzoic acid)) was added to the supernatant for 15 minutes. The absorbance of supernatant at 410 nm was measured.

Detection of the generation of ·OH.

MB was used to determine the generation of ·OH. For MOF+H_2O_2+MB group, GSH (10 mM) was incubated with MOF for 24 h. After centrifugation, H_2O_2 and MB were added into the supernatant and reacted for 2 h. Then the UV-Vis absorbance spectra of the solution were detected.

Cell culture.

4T1 cells were incubated in cell culture dishes with a diameter of 10 cm. The cells were incubated with RPMI 1640 containing 10% (v/v) fetal bovine serum (FBS), 1% penicillin and streptomycin at 37 °C in a humidified atmosphere containing 5% CO_2.

Evaluation of the intracellular ROS.

4T1 cells were cultured in confocal dishes for 24 h. The cells were divided into three groups: PBS, MOF@HA, AMGH. Each group was incubated with 1640 culture medium containing the corresponding material (100 μg/mL) for 24 h and then cultured in fresh culture medium. All the cells were incubated with 1 mL 1640 culture medium containing DCFH-DA for 30 min. The cells were washed with PBS solution and further imaged on confocal laser scanning microscope.

Detection of intracellular GPX4.

4T1 cells were seeded in confocal dishes for 24 h. The cells were divided into three groups: PBS, MOF and AMGH. The cells were incubated with 1640 culture medium

containing the corresponding material (100 μg/mL) for 24 h. Then the cells were washed and fixed with precooled 4% paraformaldehyde at room temperature for 20 min. Subsequently, each of them was treated with primary antibody and enhanced secondary antibody for 1 h, respectively. The cells were washed with PBS three times before confocal microscopy experiments.

MTT assays

4T1 cells were cultivated in 96-well plates for 24 h. Then they were divided into six groups: PBS, Light, MOF@HA, Au-MOF@HA, Au-MOF@HA+Light, AMGH+Light. The cells were incubated with different concentrations (0, 50, 100, 150, 200 μg/mL) of corresponding materials for 24 h. For the laser irradiation group, the cells were incubated with materials for 12 h and irradiated with 635 nm laser (0.5 W/cm^2) for 10 minutes and then incubated for 12 h. All the groups were washed with PBS for three times and added MTT (0.5 mg/mL, 150 μL) at 37 °C for 4 h. After removing the MTT medium, 150 μL of DMSO was added to each well. The absorbance was measured at 490 nm by a microplate reader.

Live/dead cell staining assay.

4T1 cells were seeded in confocal dishes and cultured for 24 h. The cells were divided into six groups: PBS, Light, MOF@HA, Au-MOF@HA, Au-MOF@HA+Light, AMGH+Light. The cells were incubated with different concentrations (0, 50, 100, 150, 200 μg/mL) of corresponding materials for 24 h. For the laser irradiation group, the cells were incubated with materials for 12 h, irradiated with 635 nm laser (0.5 W/cm^2) for 10 minutes and then incubated for 12 h. Subsequently, each group of cells were washed with PBS for three times and then stained with live/dead cell staining assay kit and further imaged on a confocal laser scanning microscope.

Establishment of tumor model.

Animal experiments were reviewed and approved by the Ethics Committee of Shandong Normal University, Jinan, P. R. China (approval number AEECSDNU2021074). All animal experiments were conducted and obeyed the Principles of Laboratory Animal Care (People's Republic of China) and the Guidelines of the Animal Investigation Committee, Biology Institute of Shandong Academy of

Science, China. Balb/C mice (4-6 weeks old, female, about 20 g) were fed with normal conditions of 12 h light and dark cycles and given access to food and water adlibitum. Subcutaneously injected 50 μL serum-free 1640 culture medium containing $1x10^7$ 4T1 cells into the right axillary region of Balb/ C mice. After the tumor size had reached approximately 75-100 mm^3, the mice were used in subsequent experiments.

In vivo fluorescence targeting experiment

In vivo fluorescence imaging was performed to compare the tumor targeting effect of NPs w/wo HA modification. When the tumor volume was approximately 100 mm^3, MOF@IR808@HA or MOF@IR808 (4 mg/mL, 75 μL) were intravenously injected into the 4T1 tumor bearing Balb/c mice. At different time points of 0, 3, 6, 9, 12 and 24 h post injection, the IR808 fluorescence intensity was recorded with a live body imaging system.

In vivo photothermal imaging.

The mice were intravenously injected with physiological saline, MOF@HA and AMGH (4 mg/mL, 75 μL). After 12 h of injection, the tumor site was irradiated with 635 nm laser (0.5 W/cm^2) for 10 minutes. And the temperature in the tumor site was recorded by an infrared camera.

Detection of antitumor effect of AMGH in vivo

4T1 tumor-bearing Balb/C mice were randomly divided into six groups (5 mice per group): (1) PBS, (2) Light, (3) MOF@HA, (4) Au-MOF@HA, (5) Au-MOF@HA+Light, (6) AMGH+Light. All samples were injected intravenously into the mice. After 12 h, the mice in the (3) and (4) group were irradiated by 635 nm laser (0.5 W/cm^2, 10 min). The mice continued to be fed for 14 days. The tumor volume and body weight of mice were recorded on alternate days during the experimental period. The volume of tumor was calculated as follows: volume $=W^2 \times L/2$, W= width, L= length.

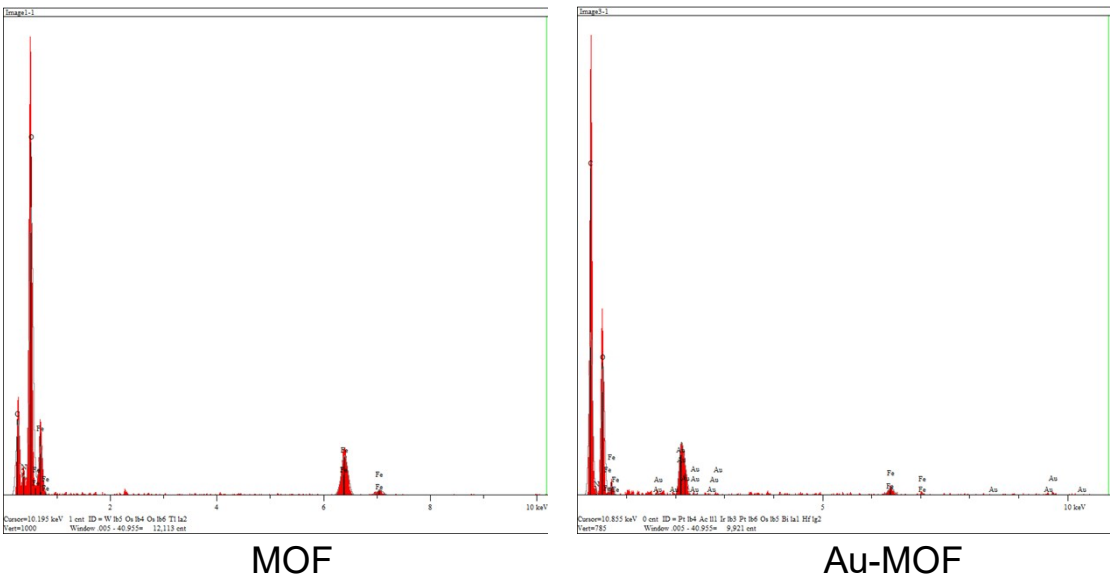

Fig. S1 EDS patterns of MOF and Au-MOF.

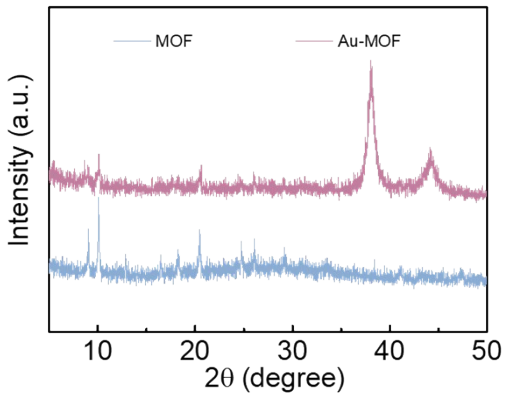

Fig. S2 XRD patterns of MOF and Au-MOF.

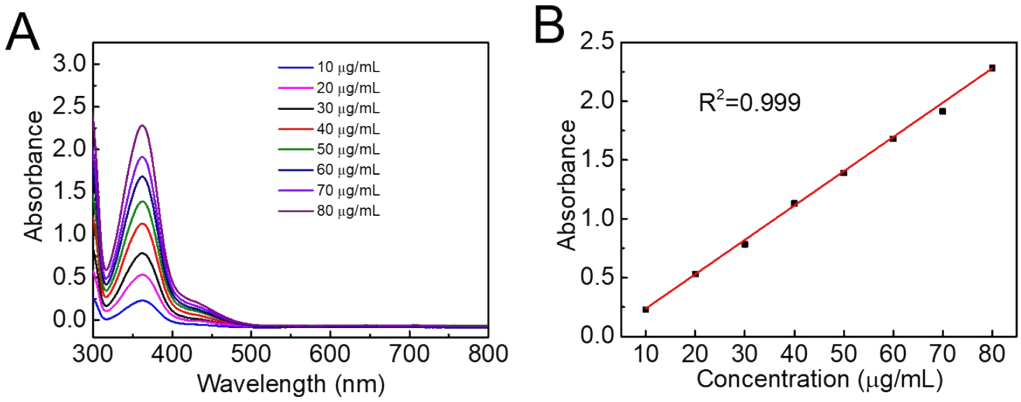

Fig. S3 The UV-Vis spectra (A) and related standard curves (B) of GA from 10-80 μg/mL.

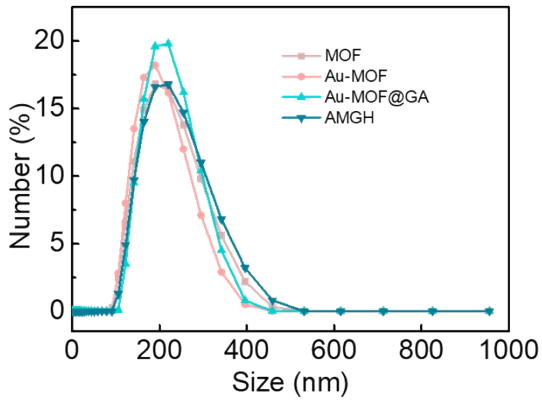

Fig. S4 The particle size distributions of MOF, Au-MOF, Au-MOF@GA and AMGH.

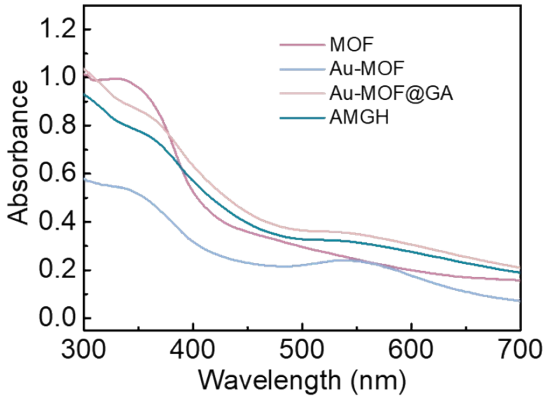

Fig. S5 UV-Vis spectrums of MOF, Au-MOF, Au-MOF@GA and AMGH.

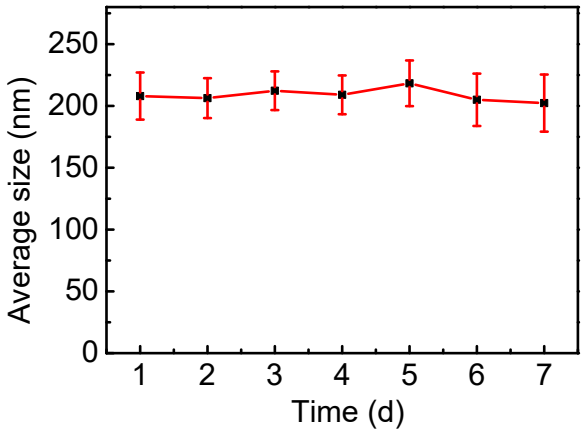

Fig. S6 Average size change of AMGH during incubation in saline for 0-7 day.

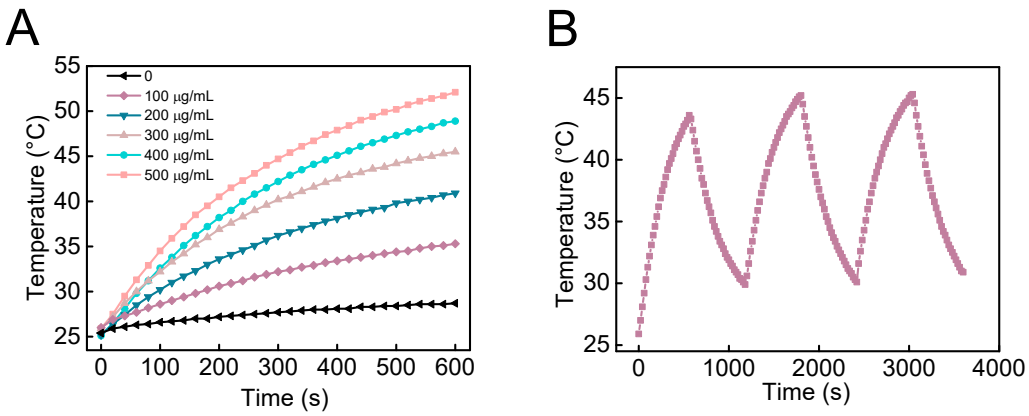

Fig. S7 (A) The photothermal curves of Au-MOF with different concentrations under 635 nm laser irradiation (0.5 W/cm^2, 10min). (B) The thermal cycles of Au-MOF (300 μg/mL) with 635 nm laser irradiation (0.5 W/cm^2).

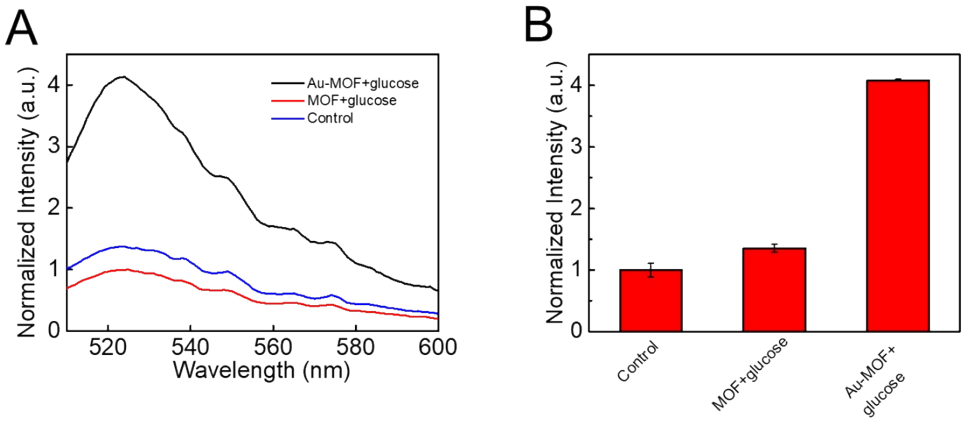

Fig. S8 The fluorescence spectrum (A) and fluorescence intensity quantization (B) of DCFH with different treatments.

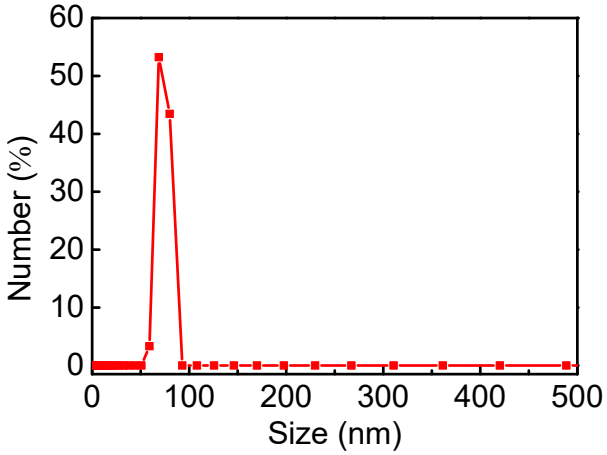

Fig. S9 DLS of AMGH with GSH treatment.

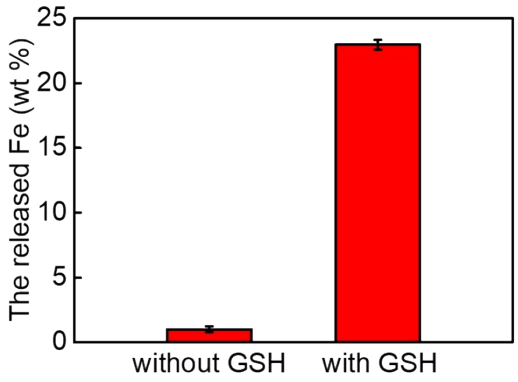

Fig. S10 The content of iron with/without GSH by ICP-AES.

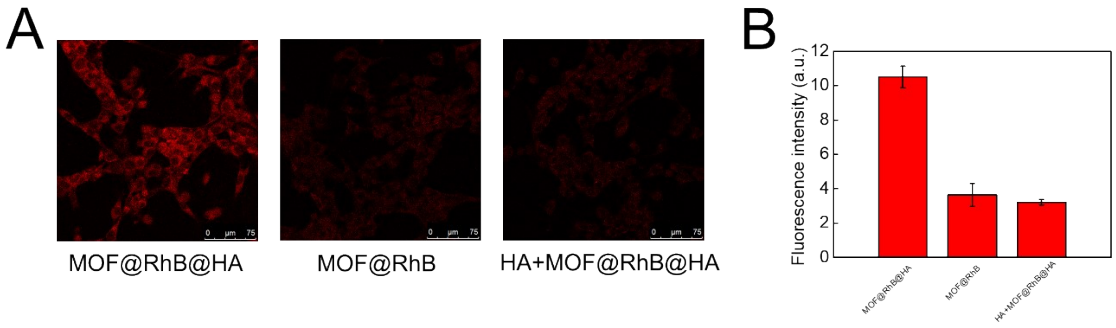

Fig. S11 (A) Confocal images of 4T1 cells co-incubated with MOF@RhB@HA, MOF@RhB, and HA+MOF@RhB@HA ("HA+" means that the cells were preincubated HA). (B) The quantitative fluorescence intensity of (A).

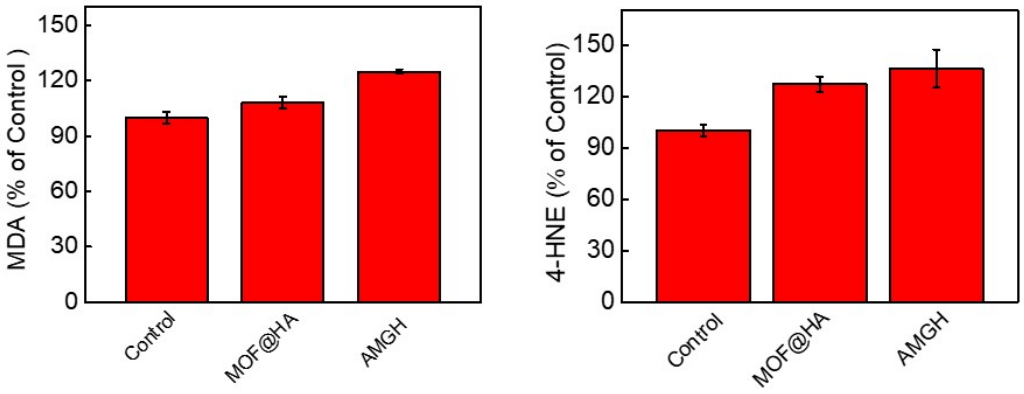

Fig. S12 The levels of MDA and 4-HNE in cells with different treatments.

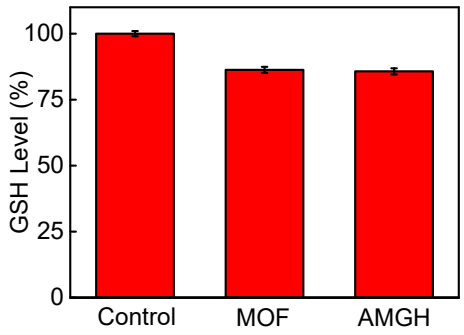

Fig. S13 The GSH levels in cell after different treatments.

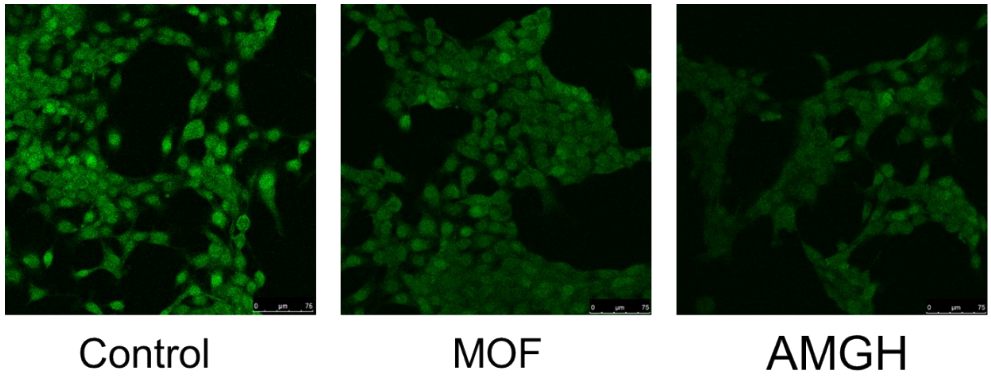

Fig. S14 Immunofluorescence assay of GPX4 after different treatments.

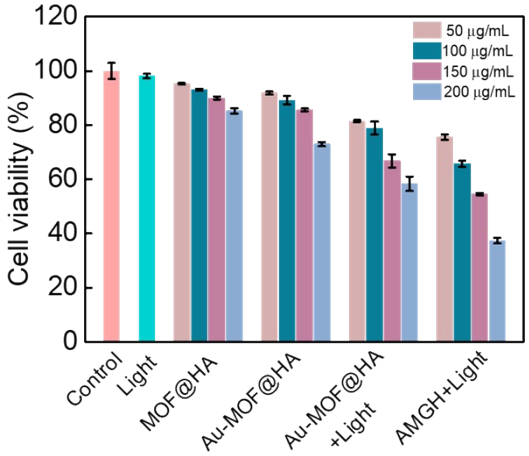

Fig. S15 MTT assay of 4T1 cells with different treatments.

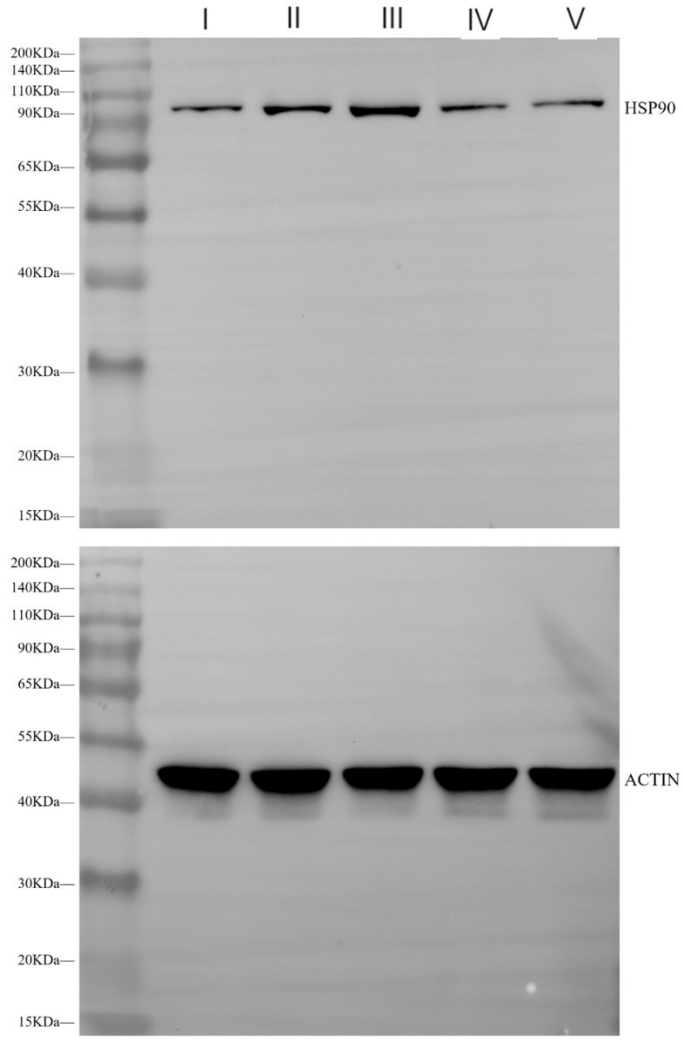

Fig. S16 The expressions of HSP90 with different treatments. (I) PBS, (II) MOF+Light, (III) Au-MOF+Light, (IV) AMGH+Light, (V) AMGH.

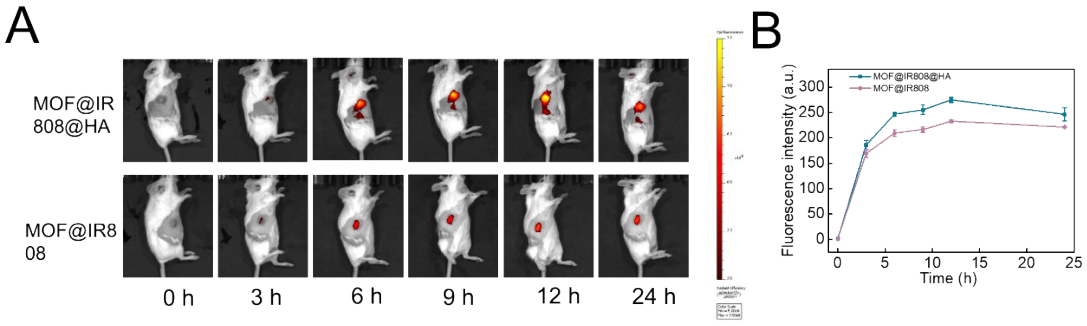

Fig. S17 (A) In vivo fluorescence imaging of mice after intravenous injection with MOF@IR808@HA and MOF@IR808 at different time points. (B) The quantitative fluorescence intensity of (A).

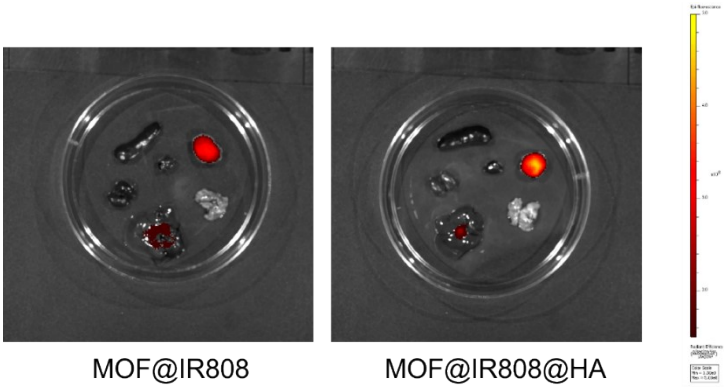

Fig. S18 The distributions of MOF@IR808@HA and MOF@IR808 in tumor-bearing Balb/c mice after intravenous injection at 12 h.

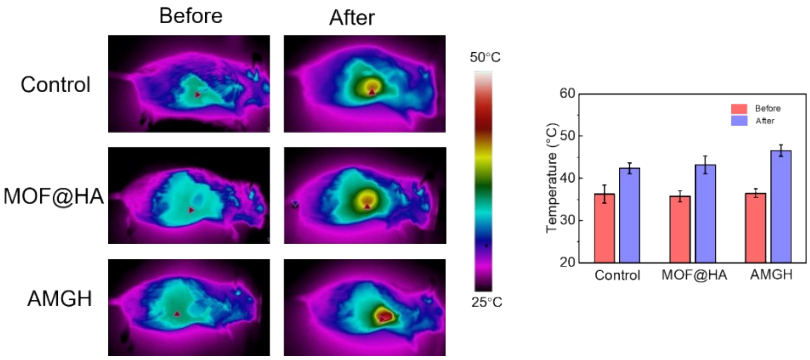

Fig. S19 The thermal images of 4T1 tumor-bearing Balb/c mice exposed to 635 nm laser irradiation at 0.5 W/cm^2 power for 10 min after intravenously injecting different materials.

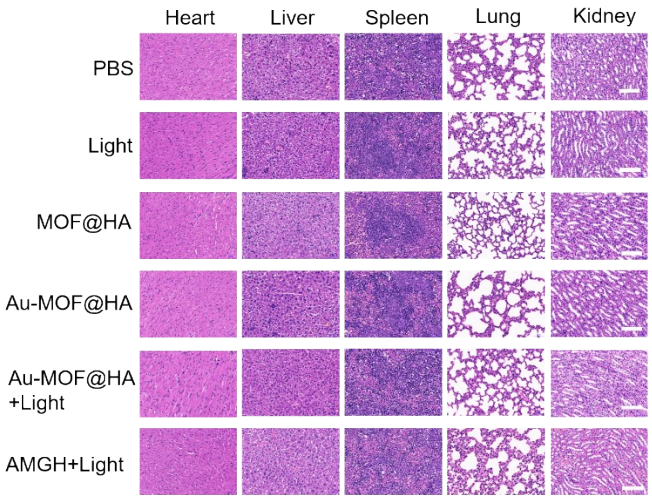

Fig. S20 The H&E staining of the main organs of mice with different treatments. Scale bars are 100 μm.