Supporting Information

Au Nanoparticles with Enzyme-Mimicking Activities Ornamented ZIF-8 for Highly Efficient Photodynamic Therapy

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Experimental

Materials

2', 7'-Dichlorofluorescin diacetate (DCFH-DA), 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-tetrazolium bromide (MTT), 4,6-diamidino-2-phenylindole (DAPI) and (9,10-Anthracenediyl-bis(methylene)-dimalonic acid) (ABDA) were obtained from Sigma-Aldrich (Saint Louis, MO). Zinc nitrate ($Zn(NO_3)_2$ $6H_2O$), 2-Methylimidazole, chloroauric acid ($HAuCl_4$), polyvinylpyrrolidone (PVP), sodium borohydride ($NaBH_4$) were acquired from Sinopharm Chemical Reagent (Shanghai, China). Chlorin e6 (Ce6) was purchased from J&K Scientific (Beijing, China). Dulbecco's modified eagle medium (DMEM) and 1% penicillin streptomycin were purchased from Thermo Fisher Scientific (Grand Island, NY).

Characterization

Fourier transform infrared (FT-IR) was collected by Perkin Elmer spectrophotometer by Nicolet 8700 (Thermo Nicolet). Transmission electron microscope (TEM) images and X-ray energy dispersive spectroscopy (EDS) were obtained on JEM-2011 operated at 200 kV. Pore size distributions were measured by ASAP2460 Accelerated surface area and porosimetry system. UV analysis was performed by UV-Vis spectrophotometry Cary 60 (Agilent, CA, USA). The size and zeta potential measurements were carried out in aqueous solution using a Malvern ZS90 dynamic light scattering (DLS) instrument. Milli-Q water (18.2 MΩ·cm) was acquired from the Milli-Q System (Millipore, Bedford, MA, USA).

Synthesis of ZIF-8 nanoparticles

In typical method for growth ZIF-8 nanoparticles in water. 2-methylimidazole (1 mL, 16.4 mg/mL), $Zn(NO_3)_2$ $6H_2O$ (20 μL, 29.7 mg/mL) and Ce6 (10 μL, 10 mg/mL in DMSO) were added into three-

necked flask with reacting 5 min at room temperature. After end of reaction, the mixture was centrifuged at 8000 rpm for 10 min to collect the precipitation, and then washed with PVP (1 mL, 10 mg/mL) for three times and redispersed in water. Then we measured the UV-Vis to calculate the content of Ce6.

Stability of ZIF-8 and Au@ZIF-8 nanoparticles

ZIF-8 and Au@ZIF-8 were suspended in PBS (pH 7.4) at 37 °C. At predetermined time points, the size of nMOFs was detected by DLS.

***In vitro* release of Ce6 from nanoparticles**

ZIF-8 and Au@ZIF-8 were suspended in phosphate buffer (PB, 0.02 M, pH 7.4 and 6.5) in the 1.5 mL tube at 37 °C in a shaking water bath. At predetermined time points, the solution was centrifuged and supernatant was measured by UV-Vis to determine the concentration of Ce6.

Cell culture

EMT-6 cells were cultured at 37 ℃ containing 5% CO_2 in the air with DMEM medium supplemented with 1% penicillin streptomycin and 10% fetal bovine serum (FBS) (HyClone, Logan, UT).

Animals and tumor model

The age of 6-8 weeks female BALB/c mice were purchased from Vital River Laboratories (Beijing, China). All animals received care in compliance with the guidelines outlined in the Guide for the Care and Use of Laboratory Animals, and all procedures were approved by the University of Science and Technology of China Animal Care and Use Committee. The tumor model was generated by injection of 2×10^5 EMT-6 cells (100 μL) into the right flank of BALB/c mice.

Statistical analysis

Statistical significance was detected by Student's t-test; significant differences between groups were indicated by *$P < 0.05$, **$P < 0.01$, and ***$P < 0.01$.

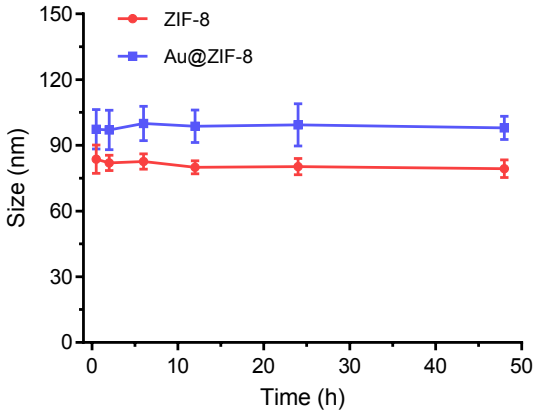

Fig. S1 Changes in size of the ZIF-8 and Au@ZIF-8 after incubation with 1x PBS.

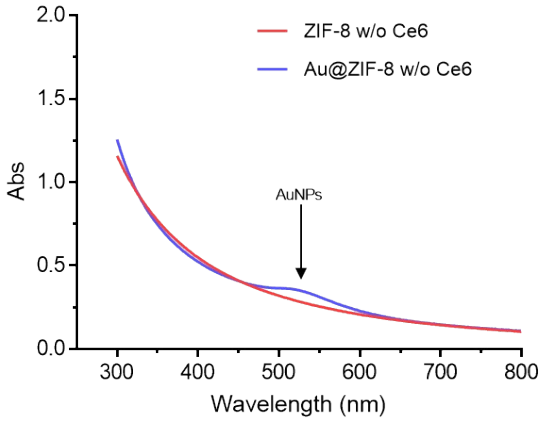

Fig. S2 UV-Vis absorption spectra of aqueous suspensions of ZIF-8 and Au@ZIF-8 both without Ce6 loading.

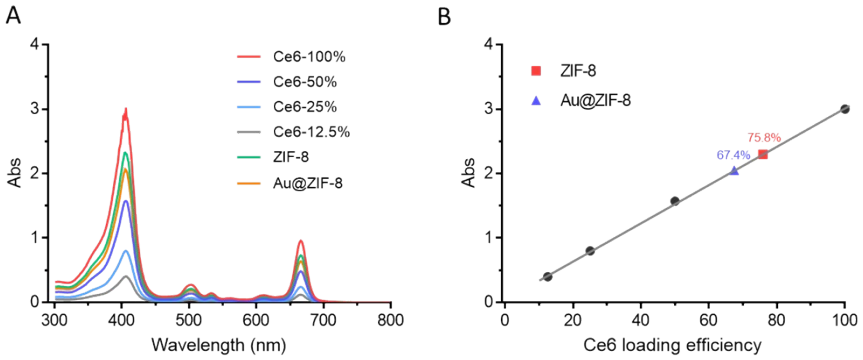

Fig. S3 (A) Absorption of different concentrations of Ce6 and purified ZIF-8 and Au@ZIF-8 and (B) the corresponding quantifications.

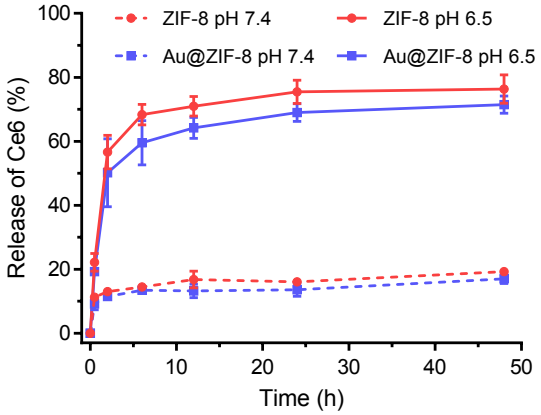

Fig. S4 Time dependent changes in Ce6 release in buffered saline of (A) ZIF-8 and (B) Au@ZIF-8 at pH 6.5 (solid lines) and 7.4 (dashed lines).

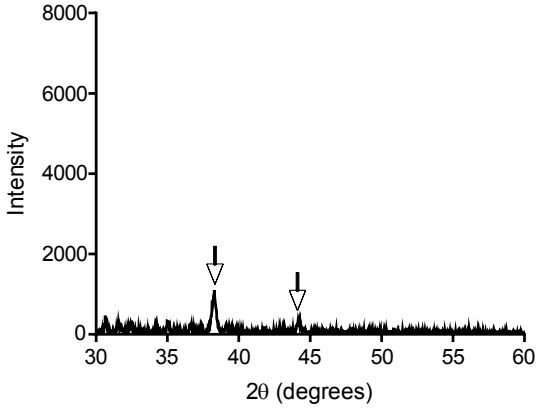

Fig. S5 XRD patterns of Au@ZIF-8 (30°-60°).

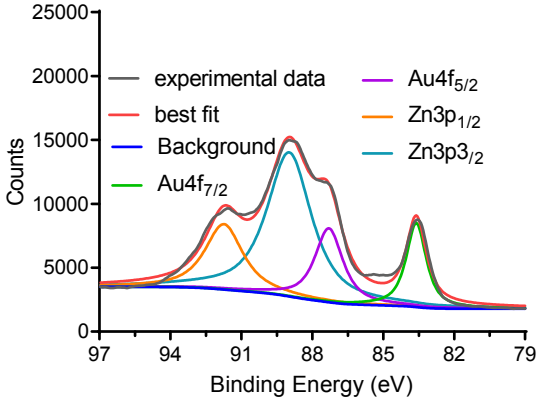

Fig. S6 XPS spectra of Au@ZIF-8 (79-97 eV).

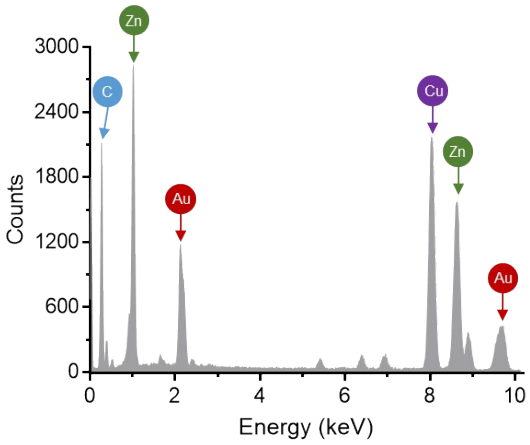

Fig. S7 Energy-dispersive X-ray spectroscopy analysis of Au@ZIF-8.

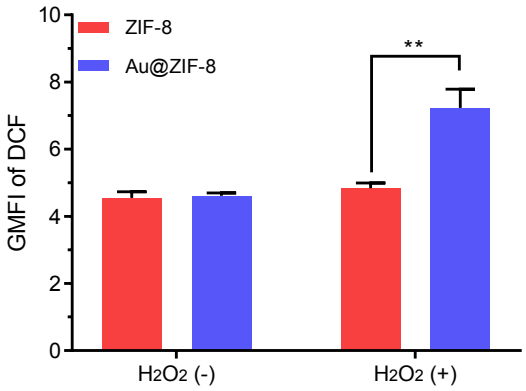

Fig. S8 Relative MFI of DCF green fluorescence from **Fig. 4C**.

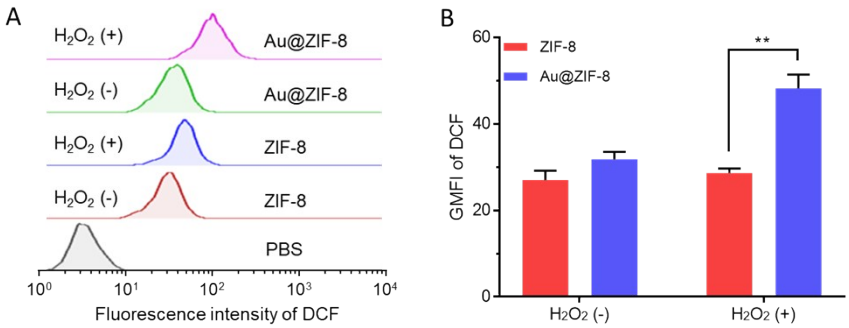

Fig. S9 (A) Intracellular $^1O_2$ measurement by FACS after cells were incubated with ZIF-8, ZIF-8+H_2O_2, Au@ZIF-8, and Au@ZIF-8+H_2O_2 and (B) Relative MFI of DCF green fluorescence from A.

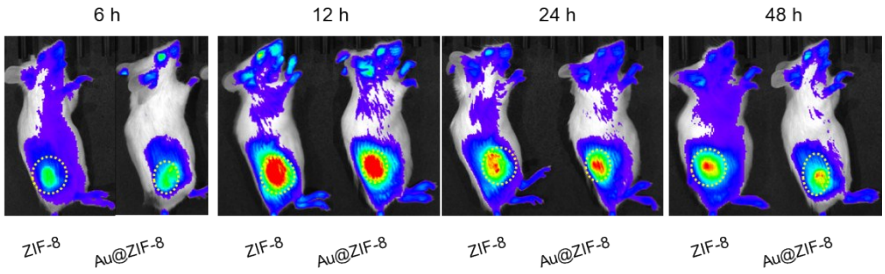

Fig. S10 Fluorescence imaging of tumor-bearing mice administered with ZIF-8 and Au@ZIF-8. Yellow circles indicate the tumor regions.

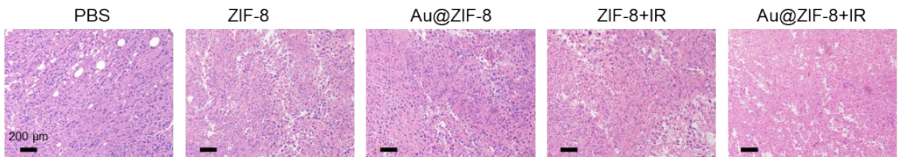

Fig. S11 Representative H&E images of the tumor slices with different treatments.