Electronic Supplementary Information

Defect-Engineered Porphyrinic Metal-Organic Framework Nanoparticles for Targeted Multimodal Cancer Phototheranostics

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Instruments and Materials

Transmission electron microscope (TEM) images were acquired from HITACHI H-7000FA TEM. The UV-visible absorption spectrum was measured with a Shimadzu UV-2600 spectrophotometer. The hydrodynamic diameter and zeta potential were observed by Dynamic light scattering (DLS) particle size analyzer (Malvern Nano-ZS90. Powder X-ray diffraction (PXRD) patterns were obtained on a Rigaku MiniFlex600 Focus Powder Diffractometer with Cu Kα line focused radiation. BET (Brunauer-Emmett-Teller) surface area analysis was performed with a Micromeritics ASAP 2420 analyzer. Laser confocal fluorescence microscope (CLSM) images were collected by Carl Zeiss NOL-LSM 710. In vivo near-infrared fluorescence images were captured using live animal imaging system (Suzhou Yingrui Optical Technology Co.). Inductively coupled plasma mass spectrometry (ICP-MS) was measured by an Analytik Jena inductively coupled plasma mass spectrometer. Unless otherwise specified, all reagents were analytical reagents purchased from commercial companies without further purification. Folate acid and DPBF were provided by Energy Chemical (Shanghai, China). 3-(4,5-Dimethyl-2-thiazolyl)-2,5-diphenyl -2H-tetrazolium bromide (MTT) and Calcein-AM/PI Double Stain Kit were purchased from Sigma-Aldrich (Shanghai, China). 2',7'-dichlorodihydrofluorescein diacetate (DCFH-DA) was purchased from Beyotime (Shanghai, China). All cell lines used in this project were from the Chinese Type Culture Collection (Wuhan University). Cell cultures were obtained from Gibco Invitrogen, including phosphate buffered saline (PBS), Dulbecco’s modified Eagle medium (DMEM), penicillin, streptomycin, and fetal bovine serum (FBS).

Synthesis of H₂TCPP

The tetrakis(4-carboxyphenyl)porphyrin (H₂TCPP) ligand was synthesized based on the previous literature¹. Methyl p-formylbenzoate (6.9 g, 0.042 mol) was dissolved in
propionic acid (100 mL) and then pyrrole (3.0 mL, 0.043 mol) was added dropwise. The reaction was refluxed for 12 h and then cooled to room temperature. The precipitate was collected by suction filtration and washed with methanol, ethyl acetate and THF respectively. Purple powder was obtained after being dried in oven overnight (Compound 1). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) (ppm) = 8.82 (s, 8H), 8.45 (d, 8H), 8.29 (d, 8H), 4.11 (s, 12H), -2.82 (s, 2H).

Compound 1 (1.5 g, 1.78 mmol) was dissolved in a mixed solution of 100 mL THF/MeOH (v/v = 1/1), then 25 mL of NaOH (2.4 g, 60 mmol) aqueous solution was added, and the mixture was refluxed for 12 h. After the reaction system was cooled to room temperature, the organic solvent was removed by evaporation under reduced pressure. An appropriate amount of water was added to the reaction solution, and then 1 M HCl was used to acidify the solution until the product precipitated completely. The precipitate was collected by filtration, washed with water and dried in vacuum oven to obtain H₂TCPP (Compound 2). \(^1\)H NMR (400 MHz, DMSO-\(d_6\)): \(\delta\) (ppm) = (s, 8H), 8.35 (m, 16H), -2.94 (s, 2H).
Synthesis of cypate

The synthesis of cypate was divided into two steps\(^2\). The first step is to synthesize 1,1,2-trimethyl-[1H]-benzo[e]indole-3-propionic acid. Mixture of 1,1,2-trimethyl-[1H]-benzo[e] indole (40.0 g, 0.19 mol) and 3-bromopropionic acid (40.0 g, 0.26 mol) in 1,2-dichlorobenzene (200 mL) was heated to 110 °C and stirred for 18 h. After the reaction was cooled to room temperature, the precipitate was collected by filtration. In order to remove unreacted materials, it was ground in dichloromethane (DCM) for 15 min, and then transferred to a vacuum drying oven to obtain 1,1,2-trimethyl-[1H]-benzo[e] Indole-3-propionic acid (Compound 3 in the reaction formula, 0.94g, yield: 52.6%).

\(^1\)H-NMR (400 MHz, DMSO-\(d_6\)): \(\delta\) (ppm) = 8.37 (d, 1H), 8.29 (d, 1H), 8.23-8.16 (m, 2H), 7.81-7.71 (m, 1H), 4.77 (t, 2H), 3.04 (t, 2H), 2.96 (s, 3H), 1.75 (s, 6H).

Synthesis of cypate: Glutaconaldehyde dianil monohydrochloride (284 mg, 1 mmol) and N, N-diisopropylethylamine (DIEA) (351 µL, 2.01 mmol) were dissolved in 2 mL DCM. The resulting suspension was placed in an ice-water bath and stirred, and then DCM (0.5 mL) solution of acetic anhydride (Ac\(_2\)O, 123 µL, 1.18 mmol) was added dropwise. The resulting clear solution was stirred for 1 hour and added dropwise with 1,1,2-trimethyl-[1H]-benz[e]indole-3-propionic acid (Compound 3, 0.82 g, 2.27 mmol)
obtained in the first step and sodium acetate (0.32, 3.9 mmol) in acetonitrile / water (9.5 / 0.5 mL). The mixture was refluxed for 16 hours, cooled, filtered, washed with acetonitrile, 5% hydrochloric acid solution and ether, and dried in vacuo to get cypate (Compound 4, 0.5 g, 70.8%). 1H NMR (400 MHz, DMSO-d6): δ (ppm) = 12.66 (br, 2H), 8.26 (d, 2H), 8.08-7.97 (m, 6H), 7.86-7.73 (m, 3H), 7.65 (t, 2H), 7.5 (t, 2H), 6.60 (t, 2H), 6.47 (d, 2H), 4.43 (t, 4H), 2.77 (t, 4H), 1.91 (s, 12H).

Synthesis of PCX-MOFs

ZrOCl$_2$.8H$_2$O (15 mg, 0.0465 mmol), H$_2$TCPP (4 mg, 0.0052 mmol), benzoic acid (140 mg, 1.15 mmol), and a certain amount of cypate (5 mg-40 mg, 0.0080 mmol-0.064 mmol) were dissolved in 5 mL DMF. The mixture was put in a 20 mL glass vial with sealed cap and reacted in an oven at 90 °C for 5 h. After cooling to room temperature, the purple precipitate was collected by centrifugation (11000 rpm, 30 min) and washed thoroughly with hot DMF solvent three times to remove unreacted cypate before lyophilization.

Cypate stability assay

Equal amounts of PC$_{20}$-MOFs and Cypate@PCN-224 were dialyzed in dialysis tubing by methanol solution (the molecular weight cut-off was 6000). The dialysate was detected by UV-vis spectrophotometer every 12 h.

UV-Vis absorbance curves of cypate and H$_2$TCPP

Cypate solutions with a concentration gradient from 0.375-12 µg mL$^{-1}$ in DMSO/water (v/v, 1/99) were prepared, and the absorbance spectra from 700-800 nm were recorded. H$_2$TCPP solutions with a concentration gradient from 0.5-3.0 µg mL$^{-1}$ in DMSO/water (v/v, 1/99) were prepared, and the absorbance spectra from 300-500 nm were recorded.

Synthesis of PC$_{20}$-MOFs-FA
2 mg FA was dissolved into 10 mL DMF solution containing 5 mg PC20-MOFs. The homogeneously dispersed suspension was stirred and reacted at room temperature for 12 h, and then washed with fresh DMF three times to remove uncoordinated FA. To determine the content of FA modified on the surface of MOF NPs, the supernatant after the first centrifugation was collected and diluted to 1/20. The UV-vis absorption spectrum of the characteristic peak at 280 nm was measured, and the content of FA was calculated to be 0.31 µM mg\(^{-1}\) via the standard linear calibration curve of FA.

**In vitro stability assay**

10 mL saline and DMEM (10%FBS) were mixed with 2 mg PC20-MOFs-FA respectively to obtain a suspension of PC20-MOFs-FA with a concentration of 200 µg mL\(^{-1}\). After the samples were incubated at 37 °C for 12 h, 24 h, 48 h, 72 h and 96 h, the size and zeta potential of the samples were measured by DLS, respectively.

**Photothermal effects of PC20-MOFs-FA**

Aqueous dispersions of PC20-MOFs-FA NPs with different concentrations (0, 50, 100, 150, 200 µg mL\(^{-1}\)) were prepared. In EP tubes, the sample (200 µL) was irradiated with 808 nm near infrared laser (1 W cm\(^{-2}\)) for 3 min, and the temperature was monitored every ten seconds by a thermal infrared camera. As described above, PC20-MOFs-FA (200 µg mL\(^{-1}\)) was irradiated under 808 nm near-infrared laser at different power (0.5, 0.75, 1, 2 W cm\(^{-2}\)) for 3 min to evaluate the photothermal effect of the nanoparticles. The heating time and natural cooling time of PC20-MOFs-FA after laser irradiation were recorded, and the photothermal conversion efficiency was calculated according to the previous literature. The calculation formula is as follow:

\[
\eta = \frac{hA(\Delta T_{\text{max, min}} - \Delta T_{\text{max,H}_2\text{O}})}{I(1 - 10^{-A808})}, \quad \tau_s = \frac{\sum m_i C_{p,i}}{hA} \]

\(\Delta T_{\text{max, min}}\) is the temperature change of PC20-MOFs-FA aqueous dispersion, \(\Delta T_{\text{max,H}_2\text{O}}\) is the temperature change of water, \(I\) is the power density of the laser, \(A808\) is the
absorption intensity of PC$_{20}$-MOFs-FA at 808 nm, $m$ is the mass, $C_p$ is the specific heat capacity, and $\tau_s$ can be calculated by the linear relationship between time and -ln($\theta$).

**Photodynamic effects of PC$_{20}$-MOFs-FA**

10 µL DMSO solution of DPBF (3.5 µg mL$^{-1}$) was added to PC$_{20}$-MOFs-FA aqueous dispersion (1 mL, 10 µg mL$^{-1}$) and ultrasonically dispersed. After irradiation with 660 nm laser (0.1 W cm$^{-2}$) or 808 nm laser (1 W cm$^{-2}$) for different times (0, 1, 2, 4, 6, 8, 10 min), the absorbance at 415 nm of samples were measured by UV-Vis spectrophotometer. The ROS generation of PC-MOFs was characterized by measuring the absorbance decrease of DPBF at 415 nm. The relative ROS production was determined as $I/I_0$ ($I_0$ refers to the absorbance intensity of DPBF at 0 min).

**Cytotoxicity assessment**

L929, HepG2, 4T1, and CT26 cells were used to evaluate cytotoxicity of NPs. Briefly, L929, HepG2, 4T1, and CT26 cells were incubated in 96-well plates for 24 h and then incubated with different concentrations (0, 25, 50, 100, 150, 200 µg mL$^{-1}$) of PC$_{20}$-MOFs-FA for 24 h. 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assays were used to detect the cell viability.

**Hemolysis assay**

The blood of BALB/c mouse was collected by anticoagulation tube and washed with PBS (300 rpm, 5 min) by centrifugation to obtain fresh red blood cells (RBCs) suspension. 4% RBCs (0.25 mL) suspension was added into PBS (0.25 mL) containing different concentrations of PC$_{20}$-MOFs-FA (0, 20, 40, 60, 80, 160 µg mL$^{-1}$), of which 0 µg mL$^{-1}$ was used as the negative control group, and deionized water (0.25 mL) was added to RBCs suspension (0.25 mL) as positive control group. Finally, all of samples were incubated at 37 °C for 6 h, and centrifuged to collect supernatant for detection of hemolysis. The absorbance of each group at 540 nm was detected by UV-vis spectrophotometer, and the hemolysis rate of PC$_{20}$-MOFs-FA was calculated as follow:
Hemolysis % = \[
\frac{\text{[(sample absorbance} - \text{negative control absorbance)}]}{\text{[positive control absorbance} - \text{negative control absorbance}]}\] \times 100\%.

In vivo biocompatibility.

In vivo biocompatibility of PC\textsubscript{20-MOFs-FA} was evaluated by hematoxylin and eosin (H&E) staining of organs and serum biochemistry test. The PC\textsubscript{20-MOFs-FA} (15 mg kg\textsuperscript{-1}) was administered to each mouse by intravenous injection, and three healthy BALB/c mice were selected as the control group. After 14 days, mice were anesthetized to collect blood. Blood supernatant harvested via centrifugation was used to analyze the serum biochemistry parameters. Three hepatic function indicators (ALT, AST, ALB), two kidney function indicators (BUN, CR) were measured. Next, the mice were sacrificed, and the main organs (heart, liver, spleen, lung and kidney) were collected for H&E staining. These analyses were provided by Wuhan Baiqiandu biotechnology Co., LTD.

Cellular uptake

After incubating 4T1 cells in a glass-bottomed dish for 24 h, they were incubated with PC\textsubscript{20-MOFs-FA} (100 µg mL\textsuperscript{-1}) for 2h, 4h, 8h, 12h, and 24h. The cells were then washed three times with PBS, and DAPI were used to stain the cell nuclei. Finally, intracellular fluorescence intensity was monitored by laser confocal microscopy.

In vitro PDT and PTT experiments

After inoculating 4T1 cells into a 96-well plate and culturing for 24 h, various concentrations of PC\textsubscript{20-MOFs-FA} (0, 25, 50, 100, 150 µg mL\textsuperscript{-1}) was added and incubated with cells for 8 h. Then, 660 nm laser (0.1 W cm\textsuperscript{-2}, 5 min) and 808 nm laser (1 W cm\textsuperscript{-2}, 5 min) were used to irradiate cells in corresponding group. After additional 24 h incubation, the cell viability was measured by MTT assays.

Calcein-AM/PI Double Staining
Cells were seeded in a 24-well plate and incubated 24 h in a CO₂ incubator. After removal of the culture medium, PC₂₀-MOFs-FA (100 µg mL⁻¹) was added and incubated with cells for 8 h. Then, 660 nm laser (0.1 W cm⁻², 5 min) and 808 nm laser (1 W cm⁻², 5 min) were used to irradiate cells in the corresponding group. The cells were incubated at 37 °C for another 4 hours, washed twice with PBS and stained with Calcein-AM (500 µL, 2 μM) and PI (500 µL, 4.5 μM) for 15 min. Finally, the cells were washed with PBS twice carefully, and imaged with a laser scanning confocal microscope. The green images of living cells were excited by 488 nm light, and the emission wavelength range was collected at 520 ± 20 nm. The red images of dead cells were excited by 514 nm light, and the emission wavelength range was collected at 640 ± 20 nm.

**Construction of 4T1 tumor-bearing mice**

Female BALB/c mice (16-18 g) were purchased from Beijing Weitong Lihua Experimental Animal Technology Co., Ltd. All animal experiments were carried out in accordance with China's Laboratory Animal Management Regulations and were approved by the Laboratory Animal Management and Use Committee of Wuhan University. After the mice were adaptively fed for 1 week, 5 × 10⁶ 4T1 cells were injected subcutaneously into the right hip joint of the mice. After tumor volume of mice reached 80 mm³ in 2-3 weeks, the experimental 4T1 tumor-bearing mice model were obtained. The formula for calculating tumor volume is as follows: tumor volume = (tumor width)² * tumor length / 2.

**In vivo multi-modal imaging**

The near-infrared fluorescence imaging system was used to record the enrichment of materials in tumors after different treatments. 808 nm (90 mW cm⁻²) laser was used as the excitation light. The emitted light was filtered through an 880 nm filter and the InGaAs camera was used to collect the fluorescence signal. PC₂₀-MOFs-FA (15 mg kg⁻¹) and PC₂₀-MOFs (15 mg kg⁻¹) were injected intravenously into 4T1 tumor-bearing mice, and NIRF images were collected at different times (2 h, 4 h, 8 h, 12 h, 24 h, 48
Similarly, 4T1 tumor-bearing mice injected with PC20-MOFs-FA (15 mg kg⁻¹) were used for photoacoustic imaging (PAI), and the PA signal at 0 h, 6 h, and 24 h post injection was captured by a high-resolution PAI instrument. Moreover, PC20-MOFs-FA (15 mg kg⁻¹) and the same amount of PBS were intravenously injected into 4T1 tumor-bearing mice. 4 h later, the photothermal imaging system was used to detect the heating effect of laser irradiation at tumor site.

**In vivo phototherapy**

When the tumors of 4T1 tumor-bearing mice reached approximately 80 mm³, the mice were randomly divided into 1-6 groups (n = 4) with treatments of: 1) PC20-MOFs-FA + 808 nm + 660 nm; 2) PC20-MOFs-FA + 808 nm; 3) PC20-MOFs-FA + 660 nm; 4) PC20-MOFs-FA; 5) PBS + 808 nm + 660 nm; 6) PBS. PC20-MOFs-FA (15 mg kg⁻¹) was injected intravenously into 4T1 tumor-bearing mice as treatment groups and PBS as the control group. It was determined by trimodal imaging that PC20-MOFs-FA reached the maximum enrichment in tumor tissue 24 h after administration. At 24 h post-injection, the different treatment groups were irradiated with 660 nm laser (0.2 W cm⁻², 5 min) or 808 nm laser (1 W cm⁻², 5 min), respectively. The tumor volume and body weight of the mice were measured every other day. After 21 days, the mice in each group were euthanized, and the tumor and main organs were sectioned.

**Statistical analysis**

The experimental data are expressed as mean ± standard deviation (mean ± SD), and two-tailed student's t test is used to compare the two groups. * P < 0.05, ** P < 0.01, and *** P < 0.001 indicated statistical difference.
Table 1. Recipes and particle sizes in the self-assembly of PCx-MOFs

<table>
<thead>
<tr>
<th>Sample</th>
<th>H$_2$TCPP (mg)</th>
<th>ZrOCl$_2$·8H$_2$O (mg)</th>
<th>BA (mg)</th>
<th>Cypate (mg)</th>
<th>Z-average (nm)$^\Delta$</th>
<th>PDI$^\Delta$</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCN-224</td>
<td>5</td>
<td>15</td>
<td>140</td>
<td>0</td>
<td>131.4 ± 0.7 nm</td>
<td>0.092</td>
</tr>
<tr>
<td>PCs$^3$-MOFs</td>
<td>4</td>
<td>15</td>
<td>140</td>
<td>5</td>
<td>136.4 ± 0.4 nm</td>
<td>0.082</td>
</tr>
<tr>
<td>PC10-MOFs</td>
<td>4</td>
<td>15</td>
<td>140</td>
<td>10</td>
<td>128.1 ± 1.2 nm</td>
<td>0.077</td>
</tr>
<tr>
<td>PC20-MOFs</td>
<td>4</td>
<td>15</td>
<td>140</td>
<td>20</td>
<td>127.8 ± 0.4 nm</td>
<td>0.069</td>
</tr>
<tr>
<td>PC30-MOFs</td>
<td>4</td>
<td>15</td>
<td>140</td>
<td>30</td>
<td>124.8 ± 1.5 nm</td>
<td>0.025</td>
</tr>
<tr>
<td>PC40-MOFs</td>
<td>4</td>
<td>15</td>
<td>140</td>
<td>40</td>
<td>272.7 ± 7.5 nm</td>
<td>0.421</td>
</tr>
</tbody>
</table>

$^\Delta$ Hydrodynamic diameter measured by dynamic light scattering in DMF.  
$^\Delta$ Polydispersity index of the particle size.  
$^\Delta$ The amount of cypate added to the one-pot synthesis.

Fig. S1. UV-Vis spectrum and the standard curve of H$_2$TCPP from 0.5-2.7 µg mL$^{-1}$.  

Fig. S2. UV-Vis spectrum and the standard curve of cypate from 0.4-12 µg mL$^{-1}$.  

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Fig. S3. TEM images of PC30-MOFs and PC40-MOFs NPs.

Fig. S4. Dynamic light scattering results for (a) PCN-224, (b) PC5-MOFs-FA, (c) PC10-MOFs-FA, (d) PC30-MOFs-FA, and (e) PC40-MOFs-FA.
Fig. S5. PXRD patterns of PC5-MOFs, PC10-MOFs, PC30-MOFs, and PC40-MOFs NPs.

Fig. S6. 400 MHz ¹H-NMR spectra of dissolved PC10-MOFs NPs, PC20-MOFs NPs, PC30-MOFs in trifluoroacetic acid-\(d\) (TFA-\(d\))/DMSO-\(d_6\) (v/v, 1/20).
Fig. S7. The ratio of cypate/H$_2$TCPP in PC$_x$-MOFs determined from standard curves.

Fig. S8. UV-Vis spectrum of cypate alone, cypate-Zr$^{4+}$ complexes and PC$_{20}$-MOFs in DMF.
Fig. S9. a) Zeta potential of PCN-224, PC20-MOFs and cypate@PCN-224. b) UV-Vis spectrum of methanol dialysate after dialysis of PC20-MOFs. c) UV-Vis spectrum of methanol dialysate after dialysis of cypate@PCN-224. d) The corresponding quantitative analysis of cypate leaking by UV-Vis spectra.

Fig. S10. The nitrogen adsorption isotherm of PC20-MOFs.
Fig. S11. UV-Vis spectra of PC$_{20}$-MOFs, PC$_{20}$-MOFs-FA, and FA.

Fig. S12. Calibration curve of folic acid in DMF at 280 nm.

Fig. S13. Zeta potential of PC$_{20}$-MOFs and PC$_{20}$-MOFs-FA NPs.
Fig. S14. a, b) Changes in the hydrodynamic particle size and PDI of PC_{20}-MOFs-FA in cell culture medium (DMEM + 10% FBS) and saline. c) Content of Zr^{4+} in PC_{20}-MOFs NPs after co-incubation with saline and cell culture medium as determined by ICP-MS.

Fig.15. The temperature changes of PC_{20}-MOFs-FA aqueous suspension (200 µg mL^{-1}) under different powers of 808 nm laser irradiation.
Fig. S16. The heating/cooling curve of PC$_{20}$-MOFs-FA aqueous dispersion under 808 nm laser (1 W cm$^{-2}$) and linear relationship between -$\ln\theta$ and time during cooling.

Fig. S17. Fluorescent inverted microscope images of ROS by 4T1 cells detected with DCFH-DA. Scale bar: 100 μm.
Fig. S18. Cell viability of L929, HepG2, 4T1, and CT26 cells incubated with various concentrations of PC$_{20}$-MOFs-FA.

Fig. S19. Image and hemolysis rate of RBCs incubated with different concentrations of PC$_{20}$-MOFs-FA at 37 °C for 6 h.

Fig. S20. H&E stained images of major organs treated with PBS or PC$_{20}$-MOFs-FA administration (15 mg kg$^{-1}$). Scale bar: 50 μm.
Fig. S21. Serum biochemical indicators of mice treated with PBS or PC$_{20}$-MOFs-FA (15 mg kg$^{-1}$).
Fig. S22. CLSM images of 4T1 cells incubated with PC$_{20}$-MOFs-FA for different times. Blue represented FL of DAPI, and green represented FL of H$_{2}$TCPP. Scale bar: 25 μm.

Fig. S23. CLSM images analysis of 4T1 cells after incubated with PC$_{20}$-MOFs-FA or PC$_{20}$-MOFs for 8 h. Blue represented FL of DAPI, and green represented FL of H$_{2}$TCPP. Scale bar: 25 μm.
Fig. S24. Cell viability of 4T1 cells under 808/660 nm laser irradiation after incubated with PC$_{20}$-MOFs-FA. (**p < 0.01).

Fig. S25. a) In vitro PA signal versus various concentrations of PC$_{20}$-MOFs-FA. b) PA images of the tumor area of 4T1 mice before and after IV injection of PC$_{20}$-MOFs-FA. The signal at 523 nm was tumor blood vessels and the signal at 744 nm was PC$_{20}$-MOFs-FA.

Fig. S26. a) Infrared thermal images and b) temperature changes of tumor area of 4T1 tumor-bearing mice treated with PBS and PC$_{20}$-MOFs-FA (15 mg kg$^{-1}$) during 808 nm laser irradiation (5 min, 1 W cm$^{-2}$).
Fig. S27. Photographs of 4T1 tumor-bearing mice 21 days after different treatments (a: PBS, b: PBS + 808 nm + 660 nm, c: PC20-MOFs-FA, d: PC20-MOFs-FA + 660 nm, e: PC20-MOFs-FA + 808 nm, f: PC20-MOFs-FA + 808 nm + 660 nm. (mean ± SD, n = 4).

Fig. S28. Body weight changes of mice received different treatments within 21 days.
References


