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Experimental

Materials: Oleic acid (OA), oleylamine (OM), Ammonium tetrathiomolybdate ($(NH_4)_2MoS_4$), Polyethylenimine (PEI, branched polymer), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC), N-hydroxysuccinimide (NHS), 2-Bromo-2-methyl-propionic acid (BMPA), Ferric acetylacetonate ($Fe(acac)_3$), benzyl alcohol were obtained from Sigma-Aldrich. Cis-Diamminedichloroplatinum (II) (cisplatin), Indocyanine green (ICG) were purchased from was purchased from Nanjing Duodian Chemical Limited Company (China). Citrate acid ($C_6H_8O_7$), chloroform, Dimethylformamide (DMF), ethanol, Succinic anhydride, hydrazine hydrate ($N_2H_4 \cdot H_2O$, 50%), nitric acid (HNO_3) were purchased from Beijing Chemical Reagent Company. All the chemical reagents and organic solvents were used as received without further treatments.

Preparation of MoS_2-PEI nanoflowers

Typically, 10 mL of aqueous solution containing 22 mg of $(NH_4)_2MoS_4$ was treated with ultrasonic bath before the addition of $N_2H_4 \cdot H_2O$. After another 40 min bath

sonication, the homogeneous mixed solution was transferred into Teflon-lined stainless steel autoclave, sealed tightly and then heated to 200 °C for 10 h.[1] Note that different sizes of MoS_2 were firstly synthesized by adjusting the concentrations of both $(NH_4)_2MoS_4$ and $N_2H_4 \cdot H_2O$ into the reaction system. Then the as-obtained MoS_2 nanoflowers were dispersed in 20 mL of PEI aqueous solution and stirred overnight to obtain MoS_2-PEI.

Preparation of MoS_2@Fe_3O_4-ICG/Pt (labeled as Mo@Fe-ICG/Pt)

The reparation and surface modification of ultrasmall Fe_3O_4 nanoparticles were conducted according to the previous reports.[2] Then 5 mL of MoS_2–PEI ethanol solution was mixed with BMPA-capped Fe_3O_4 nanocrystals under magnetic stirring to synthesize MoS_2@Fe_3O_4 nanocomposites. In order to get MoS_2@Fe_3O_4-ICG, the as-prepared MoS_2@Fe_3O_4 was redispersed into 8 mL of ICG solution (50 μg/mL) and kept stirring overnight. Pt pro-drugs (including the cis,cis,trans-diamminedichlorodihydroxy-platinum (IV)(c,c,t-Pt$(NH_3)_2Cl_2(OH)_2$ (DHP)) and cis,cis,trans-diamminedichlorodisuccinato-platinum(IV) (c,c,t-Pt$(NH_3)2Cl_2(OOCCH_2CH_2COOH)_2$ (DSP))) were prepared according to the literature[3, 4]. Then 10 mL of MoS_2@Fe_3O_4-ICG aqueous solution, 3 mg of EDC, 3 mg of NHS and 3 mg of DSP were mixed together and stirred overnight. The MoS_2@Fe_3O_4-ICG/Pt precipitates were separated by centrifugation successfully and washed carefully by deionized water. The loaded concentration of Pt pro-drug was determined by ICP-MS.

Photothermal properties of Mo@Fe-ICG

The aqueous solutions of Mo@Fe-ICG nanocomposites with different concentrations of Mo (0.1, 0.2, 0.4, 0.8 mM) were irradiated with a 808 nm laser (0.65 W cm^{-2}). The temperature changes during laser irradiation were recorded by a thermometer. For the photothermal stability test, five-rounds of 808 nm laser irradiation with power densty of 0.65 W cm^{-2} were applied on the Mo@Fe-ICG aqueous solutions by turning on/off laser device. Each cycle has 5 minutes continuous irradiation followed by a 20 minutes cooling. The temperatures during each heating cycle were also recorded by the thermometer. For the calculation of the photothermal conversion efficiency of Mo@Fe-ICG nanocomposites, both the heating curve and the cooling curve of Mo@Fe-ICG aqueous solution were recorded by a digital thermometer, and the photothermal conversion efficiency (η) of Mo@Fe-ICG was calculated according to the literature[5, 6].

Singlet oxygen detection of Mo@Fe-ICG

A kind of $^1O_2$ chemical probes, 1,4-Diphenyl-2,3-benzofuran (DPBF), were used for singlet oxygen determination of Mo@Fe-ICG nanocomposites. In detail, 1.5 mg/mL of DPBF in DMSO solution (20 μL) was mixed homogeneously with 2 mL of Mo@Fe-ICG aqueous solution (100 μM of Mo), and then irradiated under 808 nm (0.65 W cm^{-2}) for determined time. The corresponding UV-Vis-NIR absorption curves were recorded to make a comparison of the DPBF absorption intensity at 417 nm. The intracellular ROS level in Hela cells were tested by using the intracellular ROS detector of DCFH-DA. In detail, Hela cells were seeded in the six-well culture plates (5×10^4 cells per well) and cultured overnight. Then the fresh culture media containing

$MoS_2@Fe_3O_4$ or Mo@Fe-ICG nanocomposites was added. After 4 h, the cells were washed twice, and then added 1 mL of DCFH-DA diluent. After another 30 min, the cells were washed again and irradiated with 808 nm laser (1.0 W cm^{-2}) for 5 min. Finally the green emission of these treated cells was imaged by an inverted fluorescence microscope.

***In vitro* and *in vivo* MRI**

Mo@Fe-ICG aqueous solutions with different concentrations of Fe (0, 0.2, 0.4, 0.6, 0.8, 1.0 and 1.2 mM) were dispersed in 1.5 mL of centrifuge tubes before the recording of their average T_2 signal intensities. The r_2 relaxivity value was successfully calculated by the curve fitting of $1/T_2$ relaxation time as a function of Fe concentrations (mM). Also, the *in vitro* MRI imagings with different concentrations of Fe, as well as the *in vivo* MRI imagings of H22 tumor-bearing mice with/without intratumoral injection of Mo@Fe-ICG nanocomposites were obtained with the same equipment.

***In vitro* cytotoxicity of Mo@Fe-ICG/Pt**

L929 fibroblast cells or Hela cells were seeded in 96-well plates. After the overnight culture, fresh DMEM media containing $MoS_2@Fe_3O_4$, Mo@Fe-ICG or Mo@Fe-ICG/Pt nanocomposites (12.5, 25, 50, 100, 200 μM of Mo) were added. The 808 nm irradiation (1.0 W cm^{-2}) was applied for 5 min after the incubation of nanocomposites for 6 h. The treated cells were further cultured for 24 h before the final MTT test[7]. For annexin flow cytometry, HeLa cells were firstly treated with different concentrations of Mo@Fe-ICG/Pt nanocomposites. After 4 hours incubation,

808 nm laser irradiation with differnet power densities of 1, 0.5, 1.0, 1.5 W cm^{-2} was applied. The following process was similar with the literature[8], and the final results were determined by analyzing 10, 000 of ungated Hela cells with a FACS Calibur flow cytometer. For the mitochondrial membrane potential assay, Hela cells were seeded in the six-well plate and incubated overnight. Then the fresh culture media containing Mo@Fe-ICG/Pt nanocomposites was added and further cultured for 4 hours before the 808 nm irradiation (1.0 W cm^{-2}). The cells were then washed twice with PBS and incubated with JC-1 solutions for 20 min. Subsequently, 2 mL of fresh medium were added after the washing with cold JC-1 buffer solution twice. The red or green fluorescence images were detected by an inverted fluorescence microscope.

***In vivo* tumor inhibition of Mo@Fe-ICG/Pt**

Female Balb/c mice (about 20 g) were bought from the experimental animal center of Jilin University. All of the animal experiments were achieved according to The National Regulation of China for Care and Use of Laboratory Animals. Each female mouse was subcutaneously injected with H22 cells in the left axilla. After 7 days, the tumor volume reached 60-100 mm^3. Then the mice were randomly divided into seven groups (6 mice in each group), treated with i) PBS as control group; ii) 808 nm irradiation (NIR group); iii) Mo@Fe-ICG; iv) Mo@Fe-ICG/Pt; v) $MoS_2@Fe_3O_4$+NIR; vi) Mo@Fe-ICG+NIR; and vii) Mo@Fe-ICG/Pt+NIR. Note that the mice were intratumorally injected with 2 mM of nanomaterials, and received 808 nm irradiation(1.5 W cm^{-2}, 10 min) 6 hours after the injection. The mice weights and tumor sizes were recorded every two days, and the tumor volumes were calculated

with the formula of V=(tumor length)×(tumor width)^2/2. After 18 days, the tumors were dissected out and weighed carefully. The tumors as well as the main organs of each mouse were isolated and then fixed. Similarly, the *in vivo* tumor inhibition of Mo@Fe-ICG/Pt by intravenous injection was also carried out. In detail, 24 mice were assigned into four groups, then tail vein injectied with: i) 808 nm irradiation (2.5 W cm^{-2}; NIR-2 group); ii) Mo@Fe-ICG/Pt; iii) Mo@Fe-ICG/Pt+NIR-1 (1.5 W cm^{-2}, 10 min); and iv) Mo@Fe-ICG/Pt+NIR-2 (2.5 W cm^{-2}, 10 min). Note that the NIR irradiation was applied 12 hours after the intravenous injection.

Characterization: The UV-Vis-NIR adsorption spectra were carried out by a U-3310 spectrophotometer. TEM micrographs were got from a FEI Tecnai G2 S-Twin transmission electron microscope with a field emission gun operating at 200 kV. FT-IR was obtained by a PerkinElmer 580BIR spectrophotometer using KBr pellets. ICP-MS was recorded on an iCAP 6300 of Thermo Scientific. Zeta potential distribution measurements were recorded on a Zetasizer Nano ZS (Malvern Instruments Ltd., UK). MTT experiments were carried out by a microplate reader (Therom Multiskan MK3). The thermal imaging was recorded by a R300SR-HD infrared camera (NEC). All the measurements were performed at room temperature. The cells apoptosis were measured by flow cytometry (FCM, BD Biosciences).

References

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Supplementary Figures

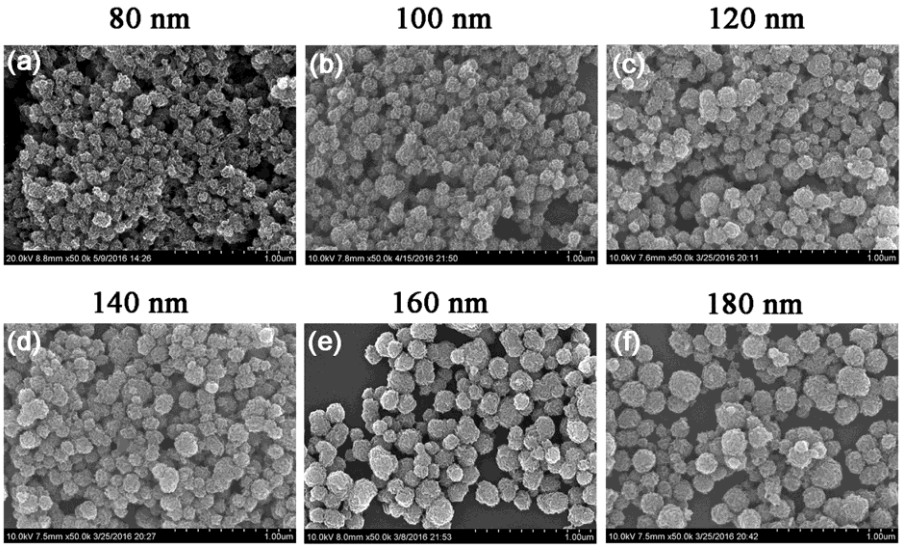

Figure S1. SEM images of MoS_2 nanoflowers with different sizes (a) 80 nm, (b) 100 nm, (c) 120 nm, (d) 140 nm, (e) 160 nm and (f) 180 nm.

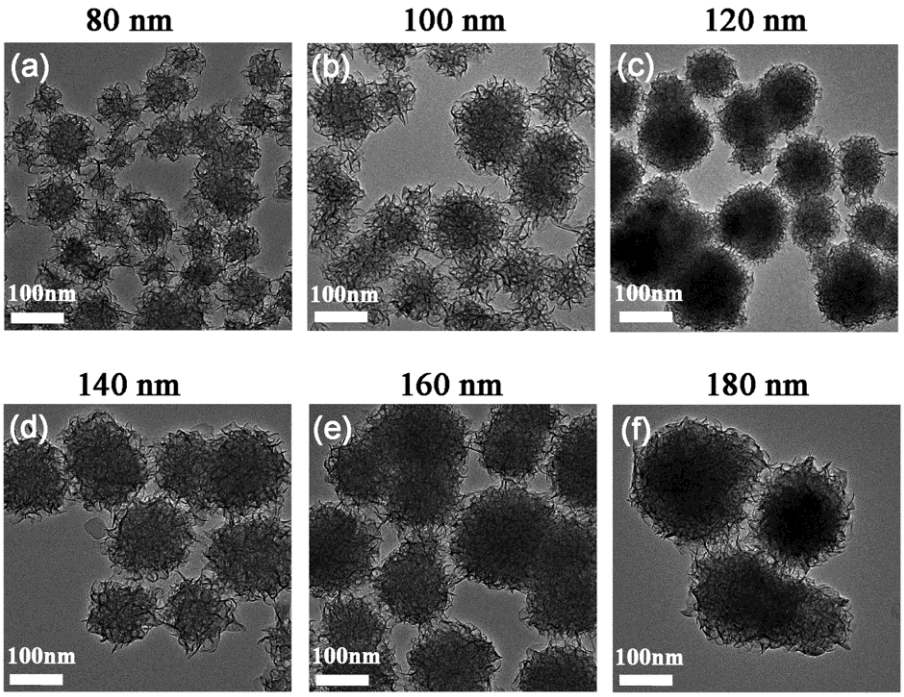

Figure S2. TEM images of MoS_2 nanoflowers with different sizes (a) 80 nm, (b) 100 nm, (c) 120 nm, (d) 140 nm, (e) 160 nm and (f) 180 nm.

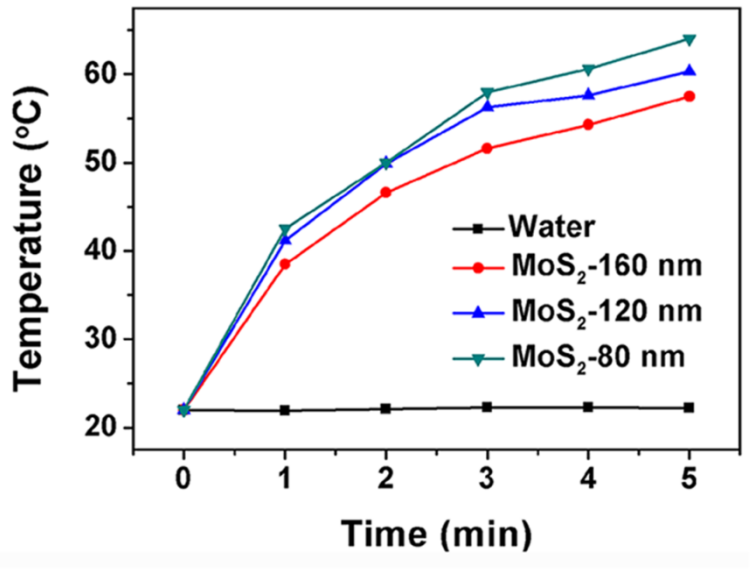

Figure S3. Temperature variation curves of MoS_2 aqueous solutions (0.4 mM of Mo) with different sizes under the irradiation of 808 nm (0.65 W cm^{-2}).

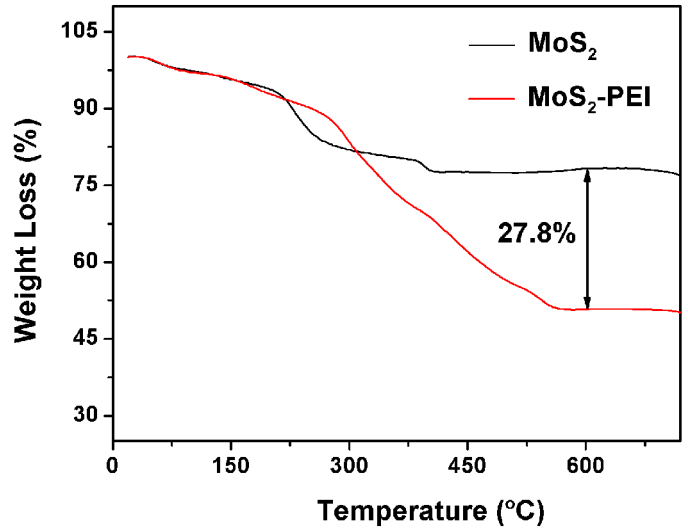

Figure S4. Thermogravimetry analysis of MoS_2 and MoS_2-PEI.

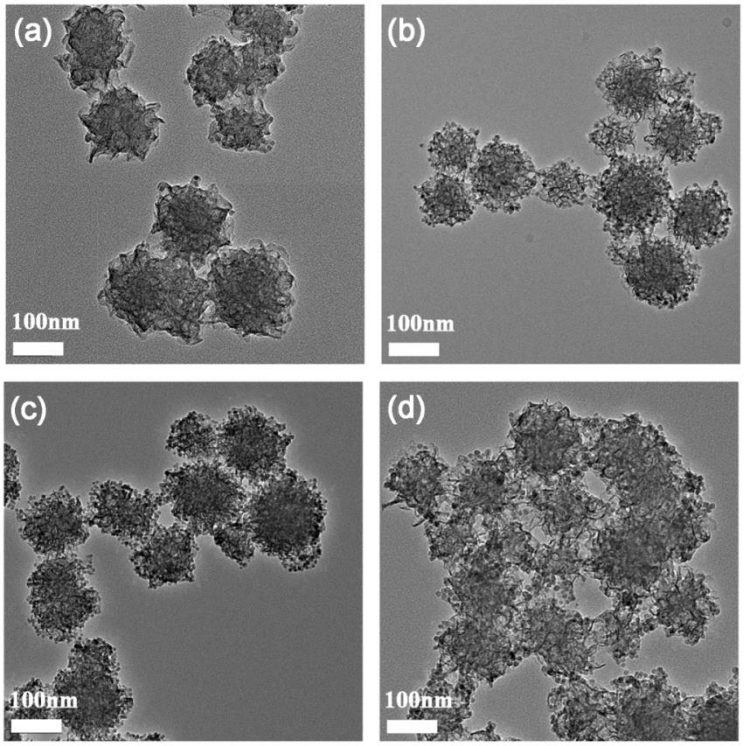

Figure S5. TEM images of MoS_2@Fe_3O_4 nanocomposites with different amount of Fe_3O_4 nanoparticles. The amount of Fe_3O_4 increased gradually from (a) to (d).

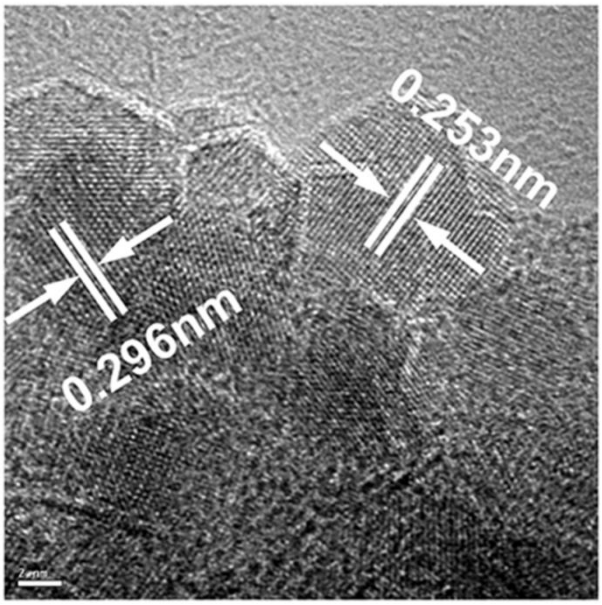

Figure S6. HRTEM image of Fe_3O_4 in MoS_2@Fe_3O_4.

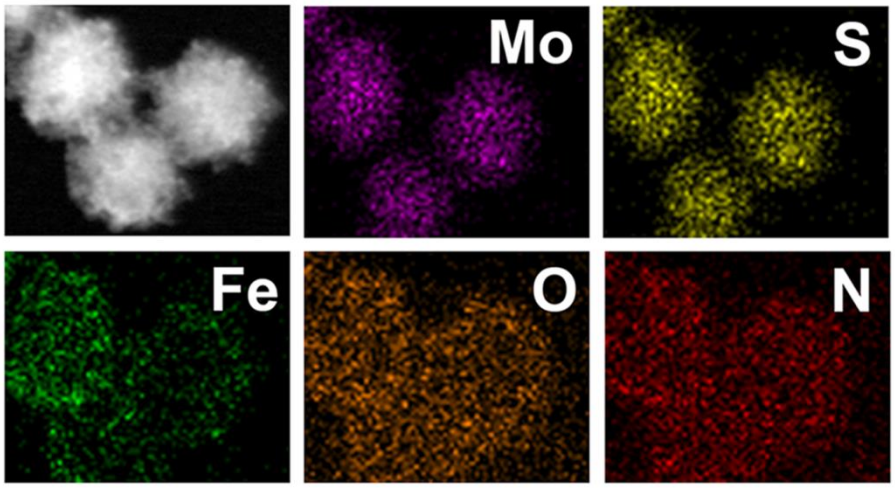

Figure S7. HAADF-STEM and HAADF-STEM-EDS mapping images of $MoS_2@Fe_3O_4$.

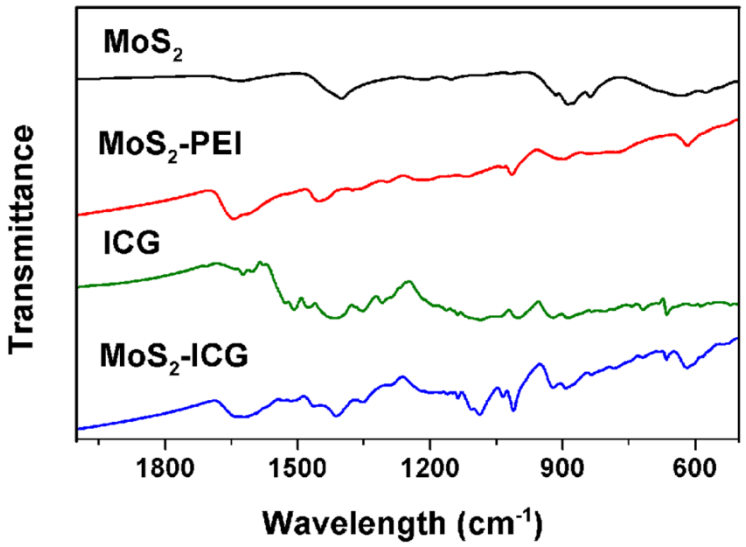

Figure S8. The FTIR spectra of MoS_2, MoS_2-PEI, ICG and MoS_2-ICG

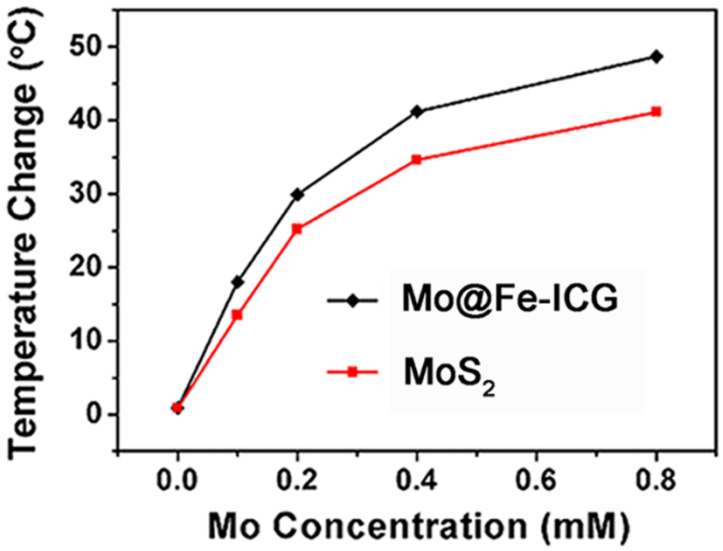

Figure S9. The temperature changes of MoS_2 and Mo@Fe-ICG aqueous solutions under the 808 nm (0.65 W cm^{-2}, 5 min).

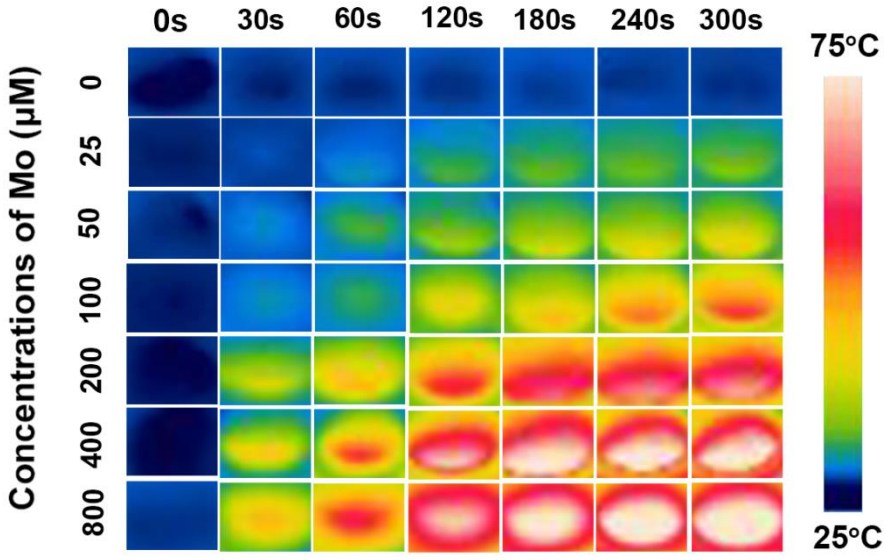

Figure S10. IR images of Mo@Fe-ICG solutions with different concentrations of Mo under irradiation power density of 0.65 W cm^{-2}.

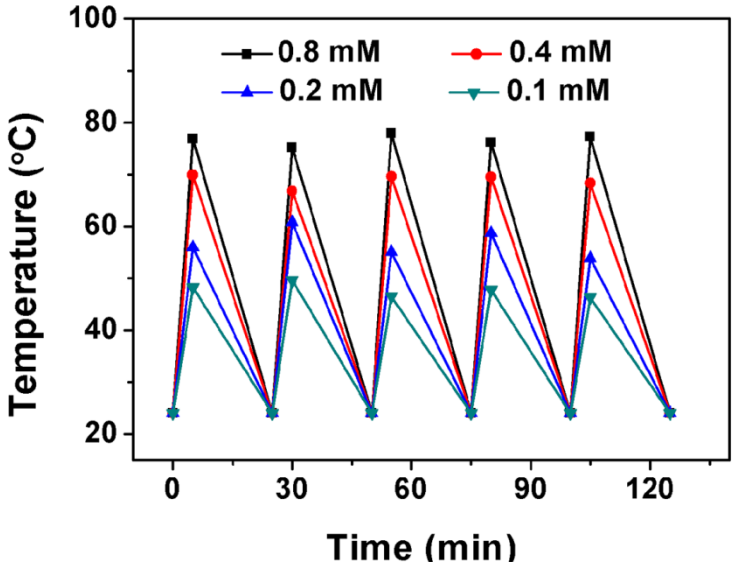

Figure S11. Temperature changes of Mo@Fe-ICG aqueous solutions with different concentrations of Mo over five ON/OFF cycles of 808 nm laser irradiation (0.65 W cm^{-2}).

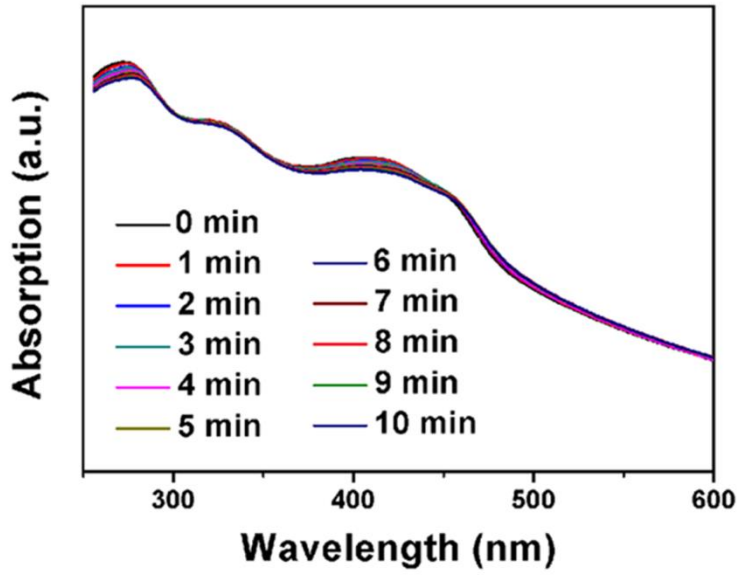

Figure S12. Absorption spectra of DPBF solution incubated with $MoS_2@Fe_3O_4$ under 808 nm irradiation for different times.

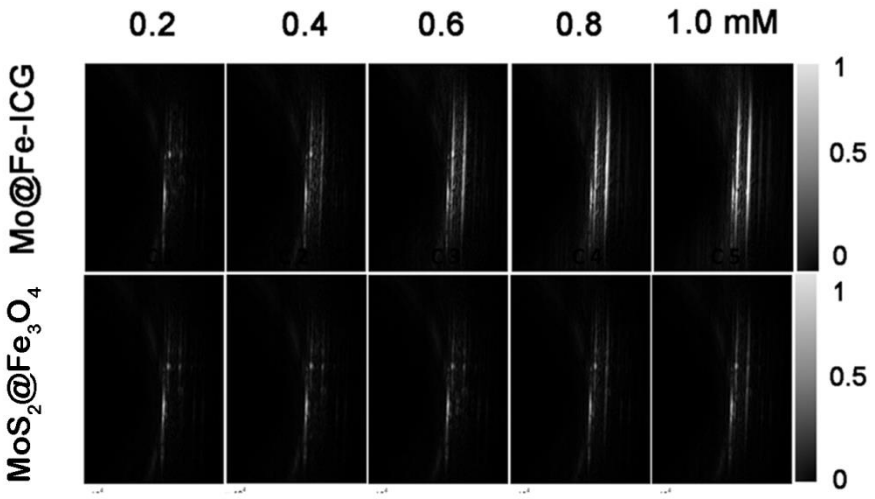

Figure S13. The PA imagings of different concentrations of $MoS_2@Fe_3O_4$ and Mo@Fe-ICG aqueous solutions (0.2, 0.4, 0.6, 0.8 and 1.0 mM of Mo).

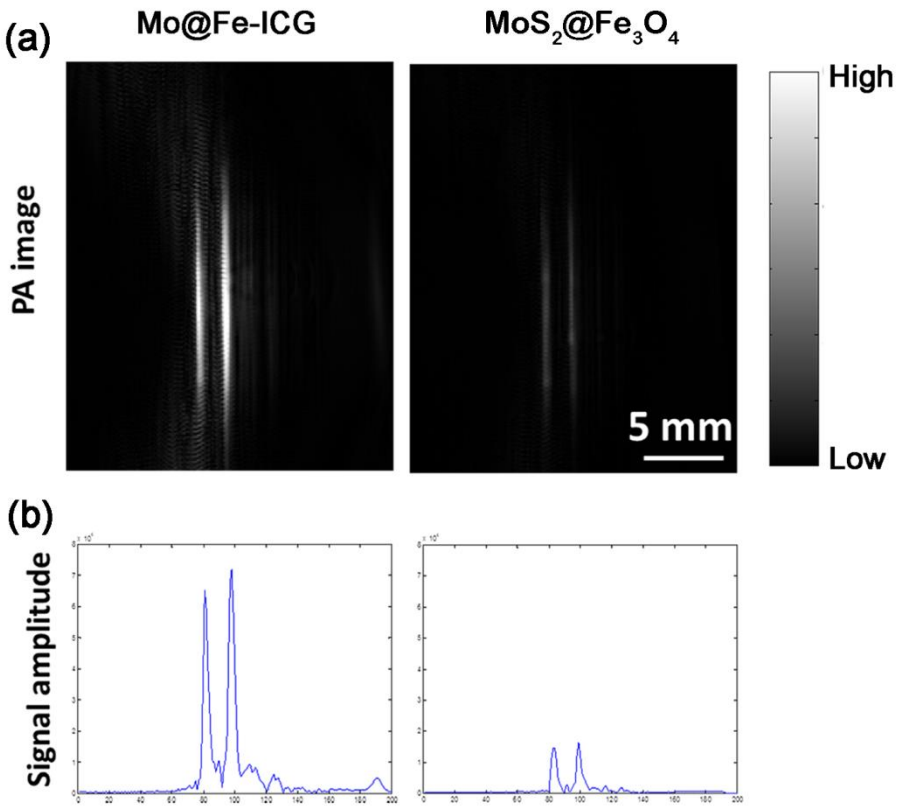

Figure S14. The PA imagings (a) and PA signals (b) of $MoS_2@Fe_3O_4$ and Mo@Fe-ICG aqueous solutions (1.0 mM of Mo).

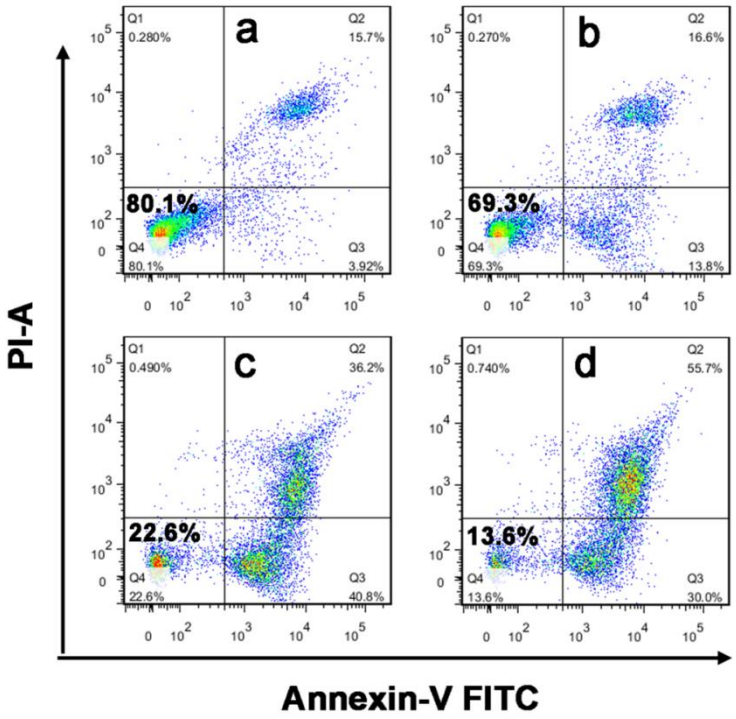

Figure S15. Apoptosis of Hela cells by staining with Annexin V-FITC and PI after 808 nm light treatment (1.0 W cm^{-2}, 5 min). The concentrations of Mo@Fe-ICG/Pt are: a: 0 μM; b: 50 μM; c: 100 μM; d: 200 μM.

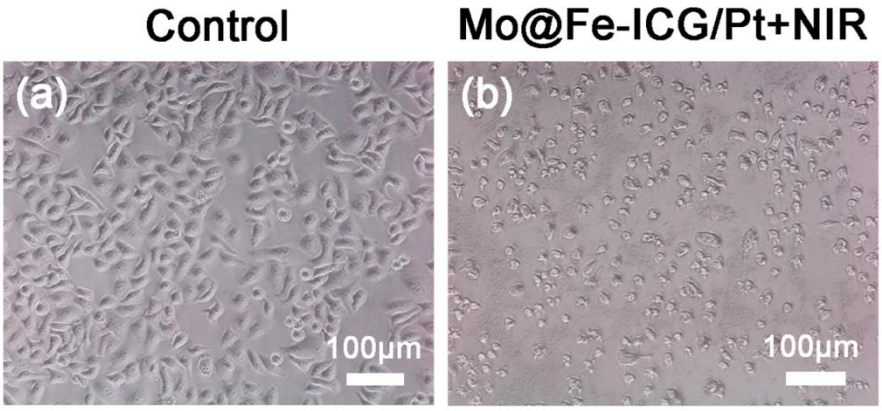

Figure S16. The fluorescence microscopy images of Hela cells after 24 h incubation: (a) control group; (b) Hela cells treated with Mo@Fe-ICG/Pt+NIR. The concentration of Mo@Fe-ICG/Pt is 100 μM, and the 808 nm NIR irradiation power density is 1.0 W cm^{-2}.

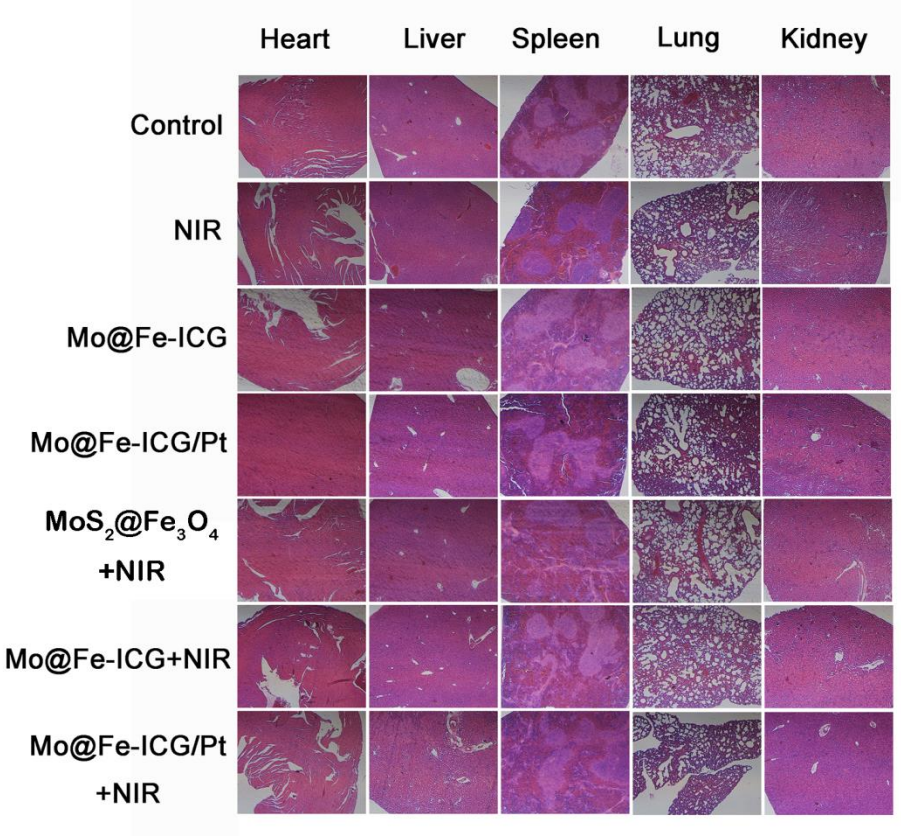

Figure S17. H&E staining images of the representative main organ slices, such as the heart, liver, spleen, lung and kidney after the intra-tumor injection of Mo@Fe-ICG (2 mM of Mo).

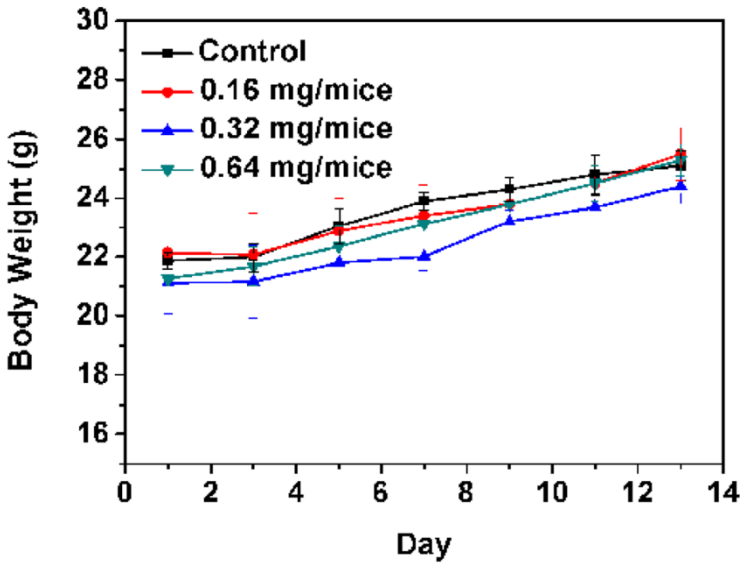

Figure S18. The body weights of Balb/c mice after tail-vein injection of Mo@Fe-ICG aqueous solutions with different concentrations of Mo.