Supplementary Information

Smart MoS_2/Fe_3O_4 Nanotheranostic for Magnetically Targeted Photothermal Therapy Guided by Magnetic Resonance/Photoacoustic Imaging

Jie Yu[1,2,#], Wenyan Yin[2,#,*], Xiaopeng Zheng[2], Gan Tian[2], Xiao Zhang[2], Tao Bao[2], Xinghua Dong[2], Zhongliang Wang[3], Zhanjun Gu[2,*], Xiaoyan Ma[1,*], Yuliang Zhao[2,*]

1. Key Laboratory of Polymer Science and Technology, School of Science, Northwestern Polytechnical University, Xi'an, Shaanxi, China

2. CAS Key Laboratory for Biomedical Effects of Nanomaterials and Nanosafety, Institute of High Energy Physics, Beijing, China

3. School of Life Science and Technology, Xidian University, Xi'an, Shaanxi, China

[#]Jie Yu and Wenyan Yin contributed equally to this study.

*Corresponding Authors: Wenyan Yin, CAS Key Laboratory for Biomedical Effects of Nanomaterials and Nanosafety, Institute of High Energy Physics, Beijing, China. E-mail: yinwy@ihep.ac.cn or Zhanjun Gu, CAS Key Laboratory for Biomedical Effects of Nanomaterials and Nanosafety, Institute of High Energy Physics, Beijing, China. E-mail: zjgu@ihep.ac.cn or Xiaoyan Ma, Key Laboratory of Polymer Science and Technology, School of Science, Northwestern Polytechnical University, Xi'an, Shaanxi, China. E-mail: m_xiao_yana@nwpu.edu.cn or Yuliang Zhao, CAS Key Laboratory for Biomedical Effects of Nanomaterials and Nanosafety, Institute of High Energy Physics, Beijing, China. E-mail: zhaoyuliang@ihep.ac.cn

Photothermal Performance Measurements

The photothermal properties of the MSIOs were measured according to the previous report [1,2]. The photothermal conversion efficiency (η) was conducted as follows: 1 mL of

MSIOs aqueous dispersion with different concentrations were exposed to 808 nm NIR laser for 10 min, and then the laser was shut off to cool to room temperature. The heating and cooling temperature trends of samples (170 ppm for MoS_2 in the MSIOs) were recorded by FLIR thermal camera. Then, the η value was calculated according to the Eq. 1:

$$\eta = \frac{hS\left(T_{\max} - T_{surr}\right) - Q_0}{I\left(1 - 10^{-A_{808}}\right)} \qquad (1)$$

Where h is the heat transfer coefficient, S is the sample container surface area, T_{max} is the steady state maximum temperature, T_{surr} is the ambient room temperature, Q_0 is the baseline energy input by the solvent and the sample container without MSIOs, I is the laser power, and A_{808} is the absorbance of MSIOs at 808 nm. The value of hS is calculated by Eq. 2:

$$\tau_s = \frac{m_d C_d}{hS} \qquad (2)$$

Where τ_s is the characteristic thermal time constant, the mass of the MSIOs solution (m_d) was g, and its heat capacity (C_d) was approximated to be 4.2 J g^{-1} k^{-1} (the heat capacity of water). The heat energy (Q_0) of the sample container and solvent without MSIOs was measured independently, using the following Eq. 3:

$$Q_0 = hS\left(T_{\max} - T_{surr}\right) \qquad (3)$$

Therefore, time constant is linear-fitted to be τ_s =237.22 s according to the linear time from the cooling period after 600 s vs $Ln\theta$ (Figure S7). Thus, based on the Eq.2, the hs is deduced to be 17.71 mW $^oC^{-1}$. Then, the η can be calculated to be 43.93 % by Eq. (3) and (1).

Supplemental Table

Table S1 Atom ratios on the surface of the MSIOs based on the XPS survey measurements in Figure 2c.

Elements	Atom Ratio. %
S 2p	10.163
Mo 3d	4.52
C 1s	40.825
O 1s	38.627
Fe 2p	5.865

Supplemental Figures

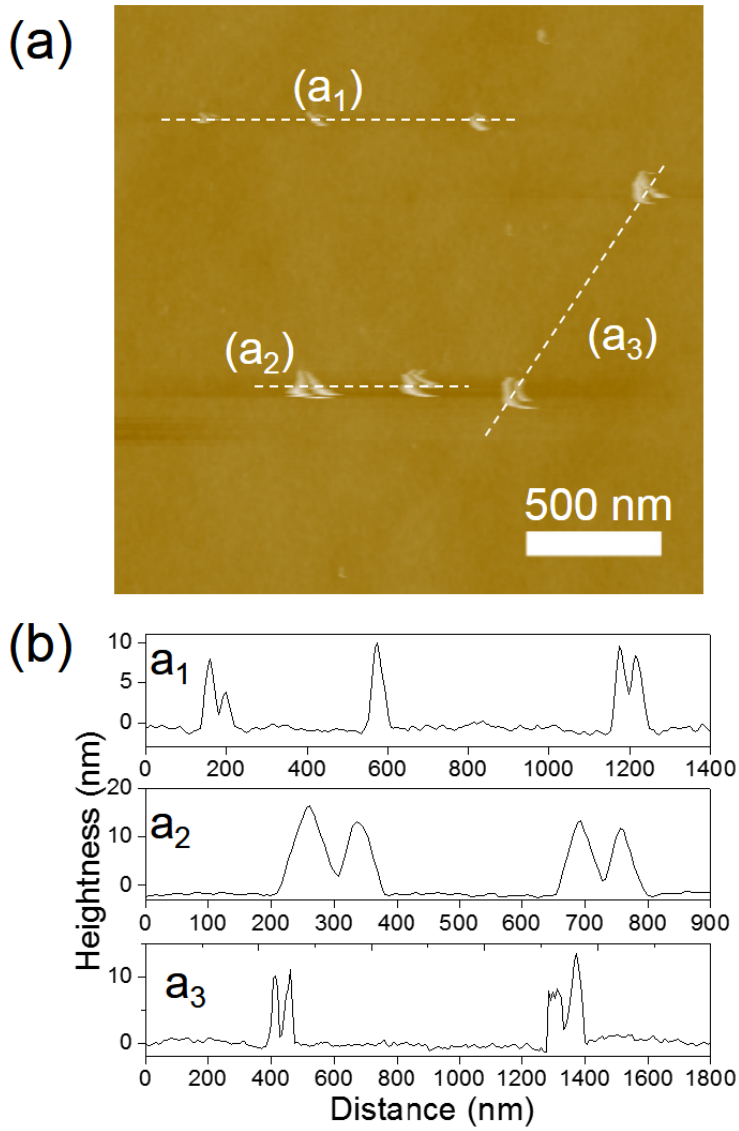

Figure S1. AFM image of (a) the MoS_2 nanoflakes with curly lamellas and (b) the corresponding lateral thickness about 8-12 nm (a_1, a_2, and a_3).

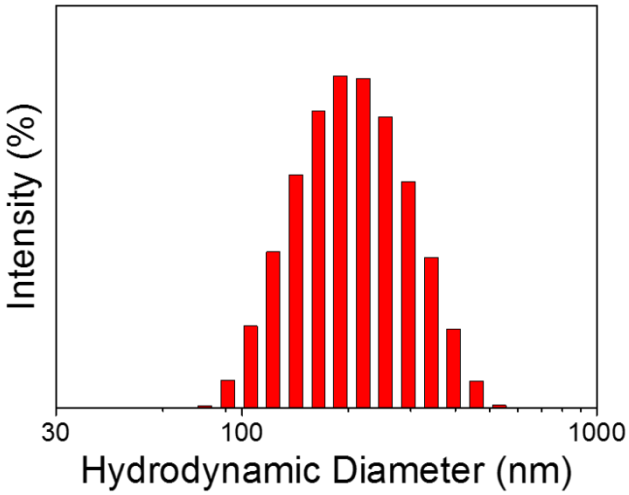

Figure S2. Hydrodynamic size of as-prepared MSIOs in water.

When the Fe^{3+} ions concentrations increased from 0.1 mmol, 0.3 mmol, to 0.6 mmol while keeping the MoS_2 nanoflakes constant, the amount of the Fe_3O_4 NPs also increased obviously, indicating that the quantity of Fe_3O_4 NPs on MoS_2 nanoflakes can be effectively tuned by the initial amount of Fe^{3+}. In addition, the Fe_3O_4 NPs are still loaded on the surface of the MoS_2 nanoflakes after being gently stirred in water for at least 3 days.

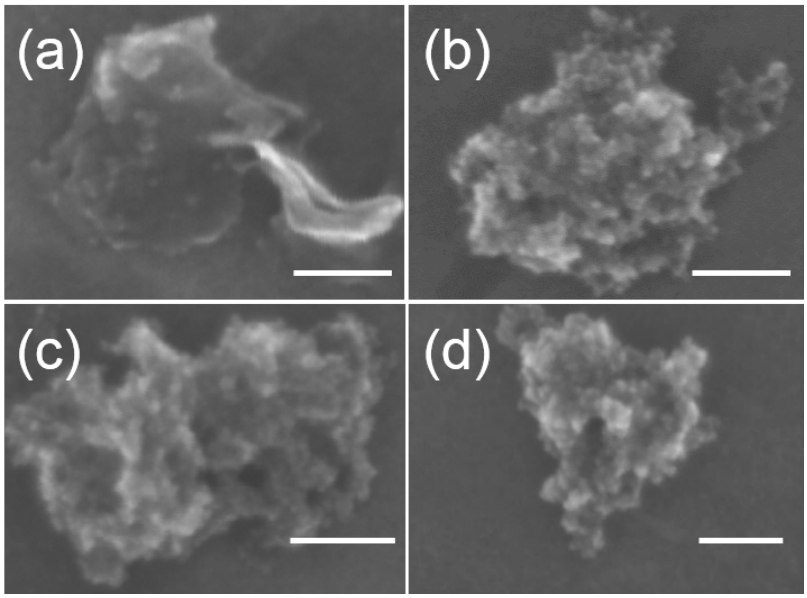

Figure S3. (a-c) MSIOs obtained from changing Fe^{3+} concentrations: (a) 0.1mmol, (b) 0.3 mmol, and (c) 0.6 mmol. (d) The MSIOs obtained from 0.6 mmol Fe^{3+} precursors after stirring in water for 3 days. Scale bar: 50 nm.

EDX spectra analysis: EDX spectra in Figure S4 further indicates that the presence of Mo and O elements signals in the MoS_2 sample, and Mo, O, Fe elements in the MSIOs sample. The Cu element was attributed to the copper grid substrate.

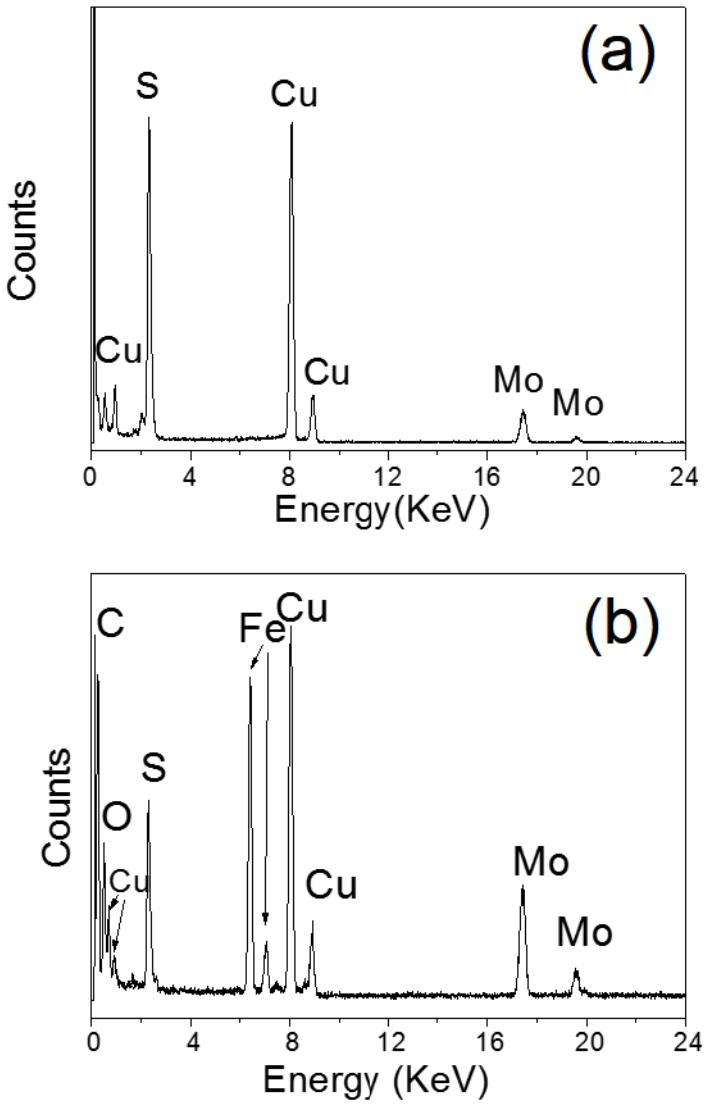

Figure S4. EDX of (a) MoS_2 nanoflakes and (b) MSIOs nanocomposite.

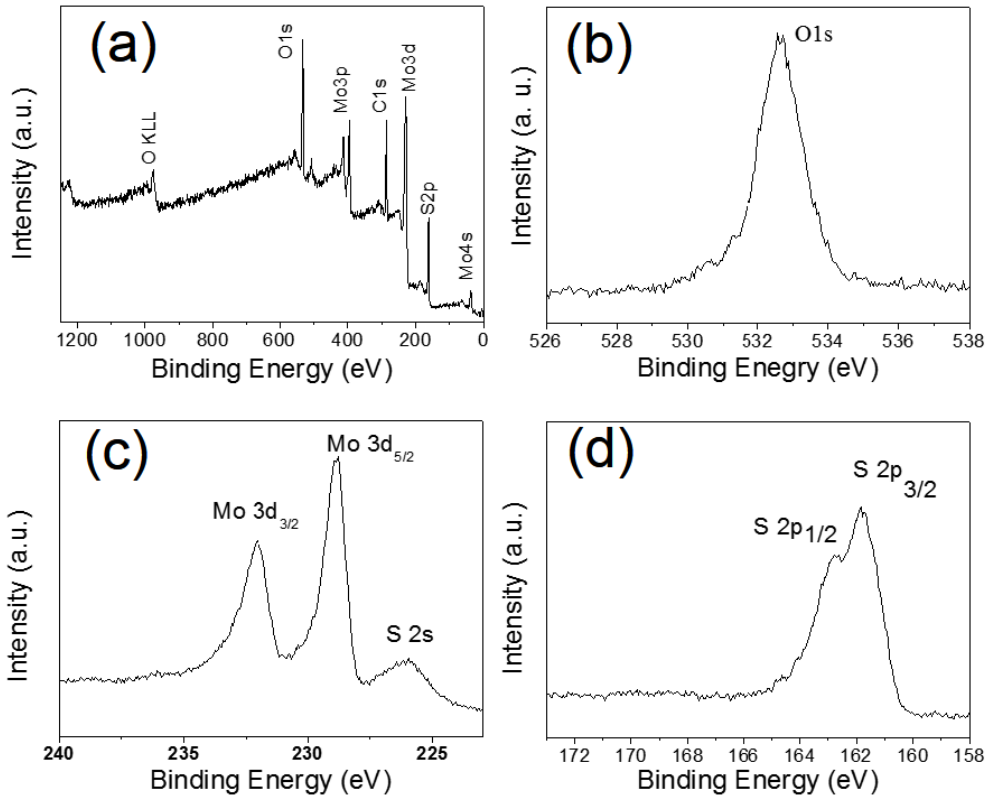

Figure S5. XPS survey plot of (a) the MoS_2 nanoflakes, and XPS spectra of (b) O, (c) Mo, and (d) S elements in the MoS_2 nanoflakes.

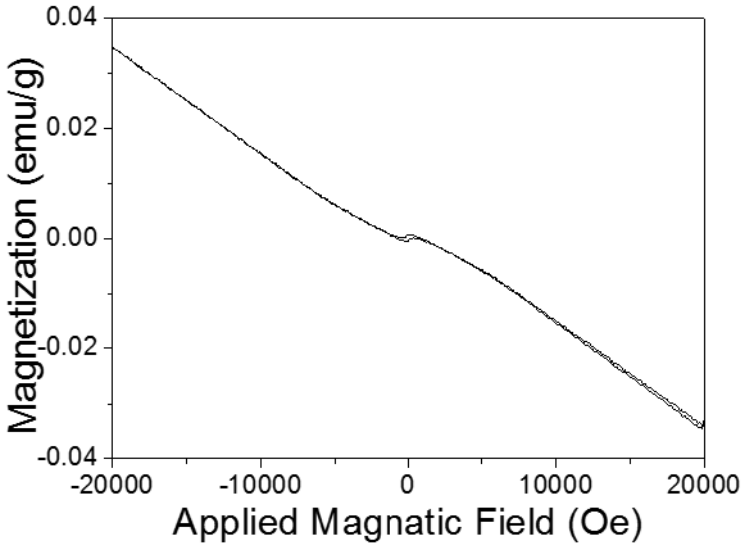

Figure S6. Magnetic Loops of MoS_2 nanoflakes. A typical magnetic response comprises both diamagnetic and the ferromagnetic terms of MoS_2 nanoflakes are observed [3].

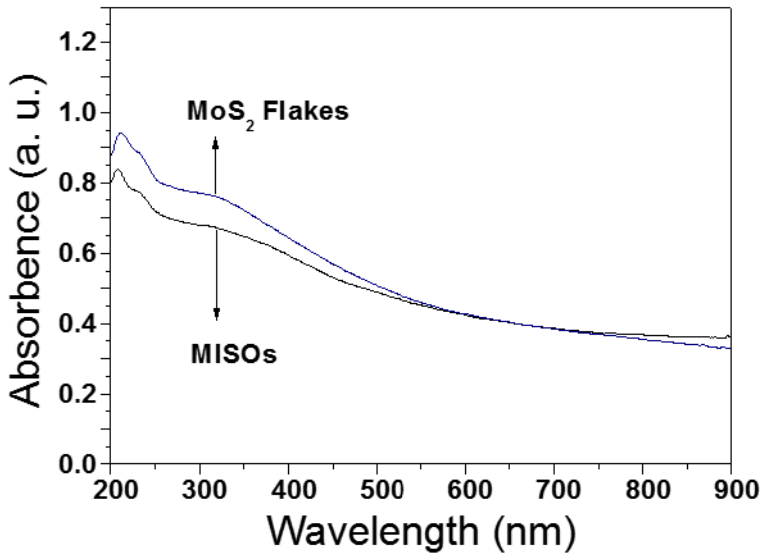

Figure S7. UV-Vis-NIR spectra of (a) MoS_2 nanoflakes and MSIOs.

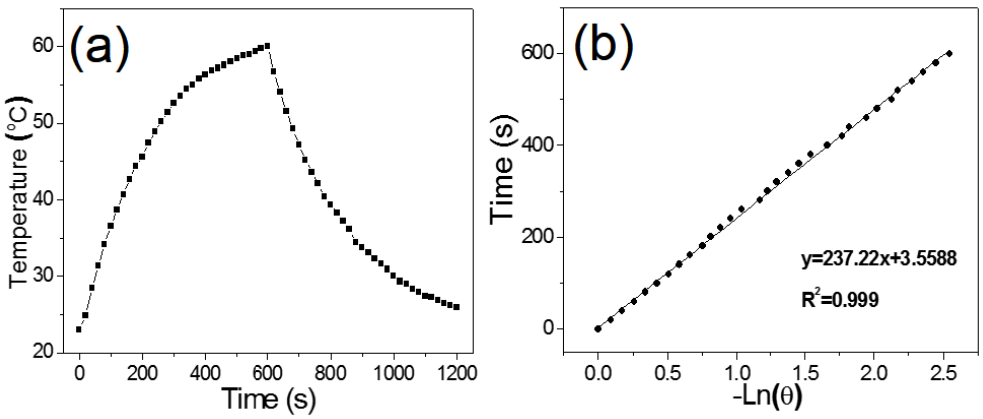

Figure S8. (a) 808-nm NIR laser induced photothermal effect f, and (b) Plot of cooling time after 10 min *versus* negative natural logarithm of driving force temperature with τ_s=237.22s of the concentration of 170 ppm.

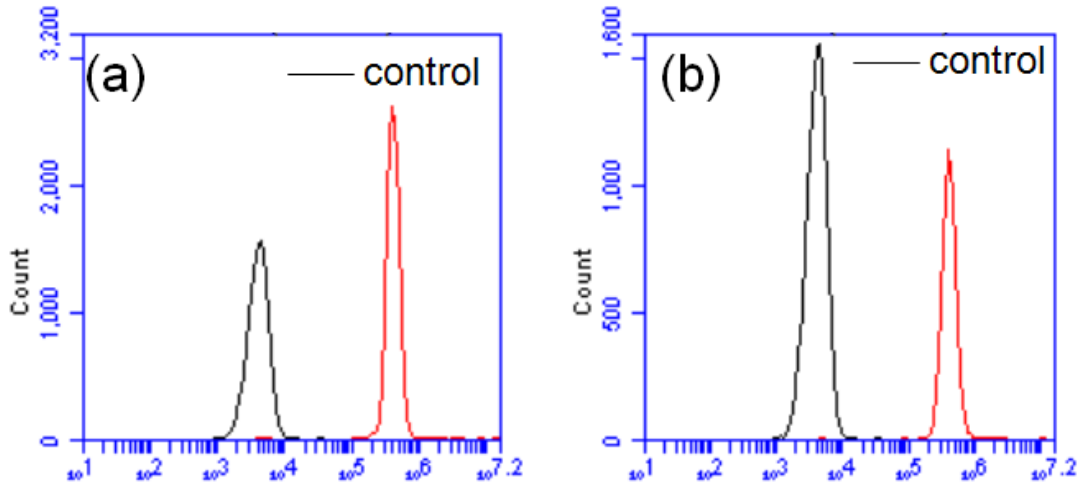

Figure S9. Flow cytometry measurements of cellular uptake levels of (a) MoS_2 nanoflakes and (b) MSIOs in Hela cells. The cells were incubated with MoS_2-FITC or MSIOs-FITC (20 μg/mL) for 4 h and cultured in fresh media at 37 ^oC, and the cells without co-incubated with materials were taken as control. (The red color in (a) and (b) show the cellular uptake levels of MoS_2 and MSIOs, respectively.)

The magnetically targeting effect were performed by using the tumor bearing mice, and the results indicated that the accumulation of MSIOs can reach ~6.9 % ID/g within 24 h, which is

obvious higher than that of the EPR induced MSIOs accumulation (4 % ID/g) in the tumor site.

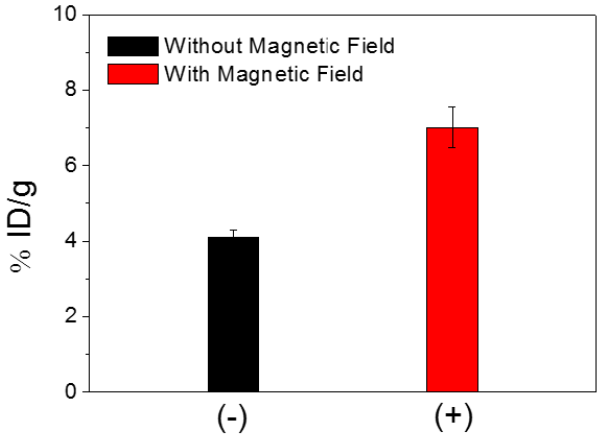

Figure S10. Biodistribution of the MSIOs induced by EPR effect (-) and magnetic targeting (+) after 24 h *i.v.* injection (determined by ICP-MS measurements of Mo element in the tumor lysates).

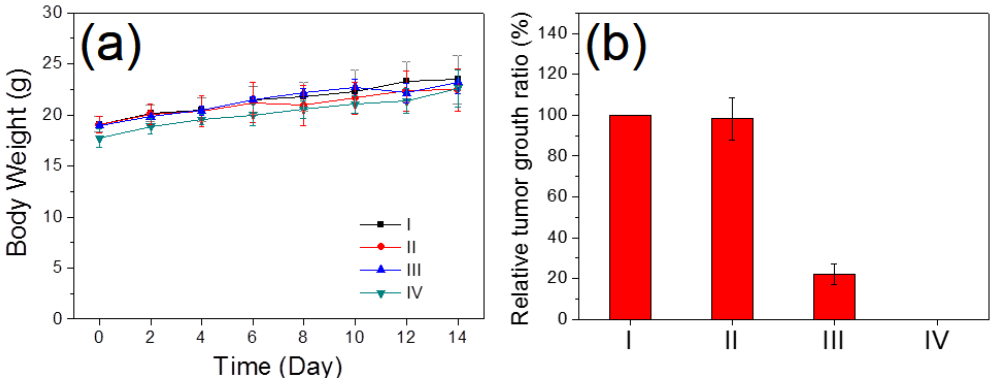

Figure S11. The body weight (a) and the relative tumor growth ratio (b) of the tumor-bearing mice from the PBS injection group (I), PBS + NIR light group (II), MSIOs + NIR laser group (III), and MSIOs + magnet targeting + NIR laser group (IV), respectively. No obvious weight loss was observed from the treated mice groups (Figure S11a), indicating that the low toxicity during the treatments *in vivo*.

Supplemental References

1. Yin W, Yan L, Yu J, Tian G, Zhou L, Zheng X, et al. High-throughput synthesis of single-layer MoS_2 nanosheets as a near-infrared photothermal-triggered drug delivery for effective cancer therapy. ACS Nano 2014; 8: 6922-33.

2. Liu X, Li B, Fu F, Xu K, Zou R, Wang Q, et al. Facile synthesis of biocompatible cysteine-coated CuS nanoparticles with high photothermal conversion efficiency for cancer therapy. Dalton Transactions 2014; 43: 11709-15.

3. Tongay S, Varnoosfaderani SS, Appleton BR, Wu J, Hebard AF. Magnetic properties of MoS_2: Existence of ferromagnetism. Appl Phys Lett 2012; 101: 123105.