Supporting Information

High-Throughput Synthesis of Single-Layer MoS_2 Nanosheets as a Near-Infrared Photothermal-Triggered Drug Delivery for Effective Cancer Therapy

Wenyan Yin,[a,,§] Liang Yan,[a,§] Jie Yu,[a,e] Gan Tian,[a,c] Liangjun Zhou,[a,d] Xiaopeng Zheng,[a,d] Xiao Zhang,[a] Yuan Yong,[a] Juan Li,[a] Zhanjun Gu,[a,*] and Yuliang Zhao[a,b*]*

[a]CAS Key Laboratory for Biomedical Effects of Nanomaterials and Nanosafety, Institute of High Energy Physics, Chinese Academy of Sciences, Beijing 100049, China

[b]National Center for Nanosciences and Technology of China, Beijing, 100190, China

[c]College of Chemistry, Sichuan University, Chengdu, 610064, China

[d]College of Materials Science and Opto-Electronic Technology, Graduate University of Chinese Academy of Sciences, Beijing 100049, China

[e]Key Laboratory of Space Applied Physics and Chemistry, Ministry of Education and Key Laboratory of Polymer Science and Technology, Shaanxi province, School of Science, Northwestern Polytechnical University, Xi'an 710129, China

[*]Corresponding Authors: zjgu@ihep.ac.cn, zhaoyuliang@ihep.ac.cn, yinwy@ihep.ac.cn

[§]These authors contributed equally.

1. Supporting Discussion

Calculation of the photothermal conversion efficiency

The photothermal conversion efficiency (μ) of MoS_2-CS was determined according to the reported method by Lu *et al*. and Hu *et al.*[1,2] The detailed calculation was given as following:

During the photothermal heating process, the total energy balance can be expressed as

$$\sum_i m_i C_{p,i} \frac{dT}{dt} = Q_{laser} - Q_{Surr} \quad (1)$$

where, m (g) and C_p (J/(g•°C)) are the mass and constant-pressure heat capacity of water, respectively, T (°C) is the solution temperature at time *t*, Q_{laser} (mW) is the energy arising from the laser irradiation, and Q_{Surr} (mW) is the energy dissipated from the system surface to the surrounding environment.

For Q_{laser}, there are two contributions. One is the energy inputted by MoS_2-CS in the dispersion, Q_{NS}, as given by equation (2),

$$Q_{NS} = I(1 - 10^{-A_\lambda})\eta \quad (2)$$

where I (mW/cm^2, 1000 mW/cm^2) is the laser power, A_λ is the absorbance of MoS_2-CS at the wavelength of 808 nm (Figure S7b), and η is the conversion efficiency from the absorbed light energy to thermal energy.

The other is the absorbance by the cuvette walls and the solution, Q_{Dis} (mW). It is measured independently to be 29.89 mW using pure water without MoS_2-CS. So, we obtain

$$Q_{laser} = Q_{NS} + Q_{Dis} = I(1 - 10^{-A_\lambda})\eta + 29.09 \quad (3)$$

In addition, the energy dissipation is usually expanded as Taylor series of ΔT. In our experiment, the first term is employed, which gives

$$Q_{Surr} = hS\Delta T = hS(T - T_{Surr}) \quad (4)$$

Where *h* (mW/(m^2•°C)) is heat transfer coefficient, *S* (m^2) is the surface area of the container, and T_{Surr} is ambient temperature of the surroundings.

When the heat input is equal to heat output, the system reaches the steady state, and the temperature rises to a maximum, T_{Max} (°C). In this case, the left side of Equation (6) becomes zero, we then obtain

$$Q_{laser} = Q_{Surr} \quad (5)$$

Combining Equation (2-5), η is therefore given by

$$\eta = \frac{hS(T_{Max} - T_{Surr}) - Q_{Dis}}{I(1 - 10^{-A_{808}})} \quad (6)$$

To get the *hS*, we herein introduce θ using the maximum system temperature, T_{max}

$$\theta = \frac{T - T_{Surr}}{T_{Max} - T_{Surr}} \quad (7)$$

and a sample system time constant τ_s (s)

$$\tau_s = \frac{\Sigma_i m_i C_{p,i}}{hS} \quad (8)$$

Substituting Equation (6-7) into Equation 1, we obtain

$$\frac{d\theta}{dt} = \frac{1}{\tau_s}\left[\frac{Q_{NS} + Q_{Dis}}{hS(T_{Max} - T_{Surr})} - \theta\right] \quad (9)$$

At the cooling stage of the aqueous dispersion of MoS_2-CS, the laser was shut off, the $Q_{NS}+Q_{Dis}=0$. In this case, Equation (9) becomes

$$dt = -\tau_s \frac{d\theta}{\theta} \quad (10)$$

Integrating Equation (10), we obtain

$$t = -\tau_s \ln\theta \quad (11)$$

Therefore, time constant is determined to be τ_s=202.75 s by applying the linear time data from the cooling period (after 600 s) vs-Lnθ (Figure 3c,d). Afterwards, according to Equation (11), the hS is deduced to be 10.36 mW/°C. Substituting 10.36 mW/°C into Equation (5), the 808 nm laser heat conversion efficiency (η) of MoS_2-CS can be calculated to be 24.37%.

References

[1] Tian, Q.; Jiang, F.; Zou, R.; Liu, Q.; Chen, Z.; Zhu, M.; Yang, S.; Wang, J.; Wang, J.; Hu, J. Hydrophilic Cu_9S_5 Nanocrystals: A Photothermal Agent with a 25.7% Heat Conversion Efficiency for Photothermal Ablation of Cancer Cells *in Vivo*. *ACS Nano* **2011**, *5*, 9761-9771.

[2] Liu, Y.; Ai, K.; Liu, J.; Deng, M.; He, Y.; Lu, L. Dopamine-Melanin Colloidal Nanospheres: An Efficient Near-Infrared Photothermal Therapeutic Agent for *In Vivo* Cancer Therapy. *Adv. Mater.* **2013**, *25*, 1353-1359.

2. Supporting Figures

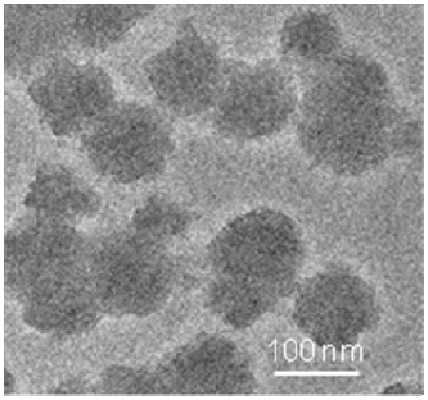

Figure S1. Typical TEM image of MoS_2-CS nanosheets.

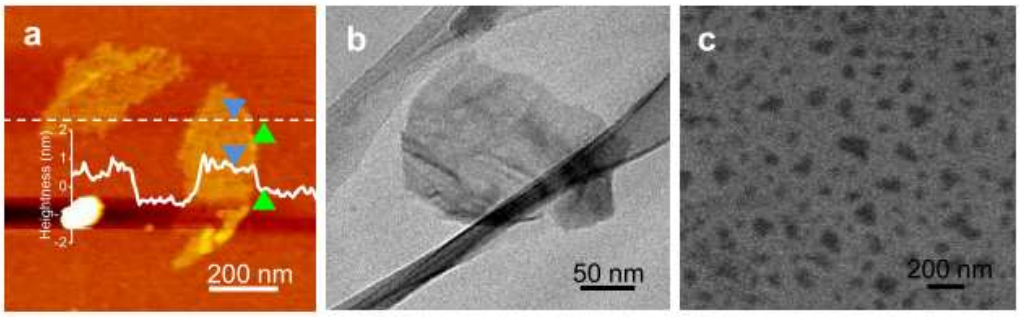

Figure S2. Typical (a) AFM, (b) TEM, and (c) SEM images of MoS_2 nanosheets prepared *via* sonication for 1 h. This result showed that MoS_2-based nanosheets could be obtained by changing the sonication time.

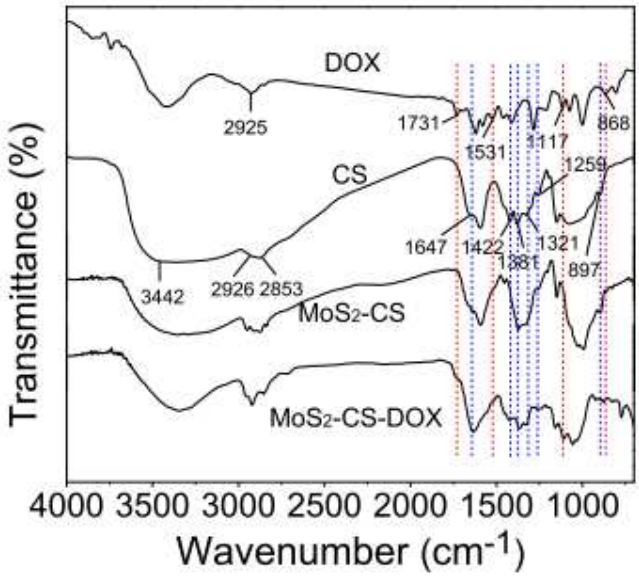

Figure S3 FT-IR spectra of DOX, CS, MoS_2-CS and MoS_2-CS-DOX, respectively. For MoS_2-CS, the peak appearing at 3442 cm^{-1} was due to the stretching vibration of N-H bond. Both the -CH_2- strength vibration (2840-2960 cm^{-1}) and the internal vibration of the amide bonds (1320-1650 cm^{-1}) of CS molecules were also observed in the FT-IR of MoS_2-CS. These results indicated that CS molecules were successfully attached onto the surface of MoS_2 nanosheets. After DOX molecules were further adsorbed on the MoS_2-CS nanosheets, the additional absorption band were observed at 1731 cm^{-1}, which was attributed to the carbonyl peaks of DOX. The peak centered at 868 cm^{-1}corresponded to primary amine -NH_2 wag vibration from DOX. These observations further confirmed the successful loading of DOX to MoS_2-CS. The obtained results were also in good agreement with an earlier report.

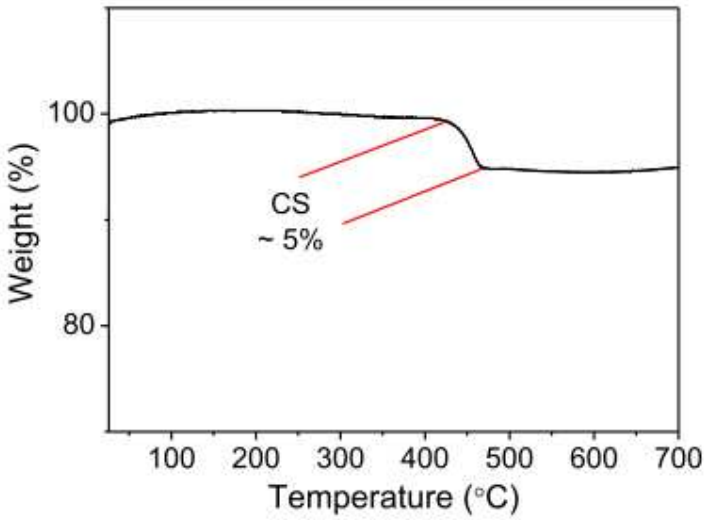

Figure S4. Thermal gravimetric (TGA) analysis of the MoS_2-CS nanosheets. The weight-loss region (400-450 ℃) should be attributed to the decomposition of CS molecules. The amount of CS molecules was determined to be *ca.* 5 *wt*%, indicating that CS molecules were really adsorbed on the surface of MoS_2-CS.

Figure S5. A large amount of with whole volume of 100 ml of MoS_2-CS dispersed in deionized water for more than 20 days. The concentration is ~1.0 mg/ml.

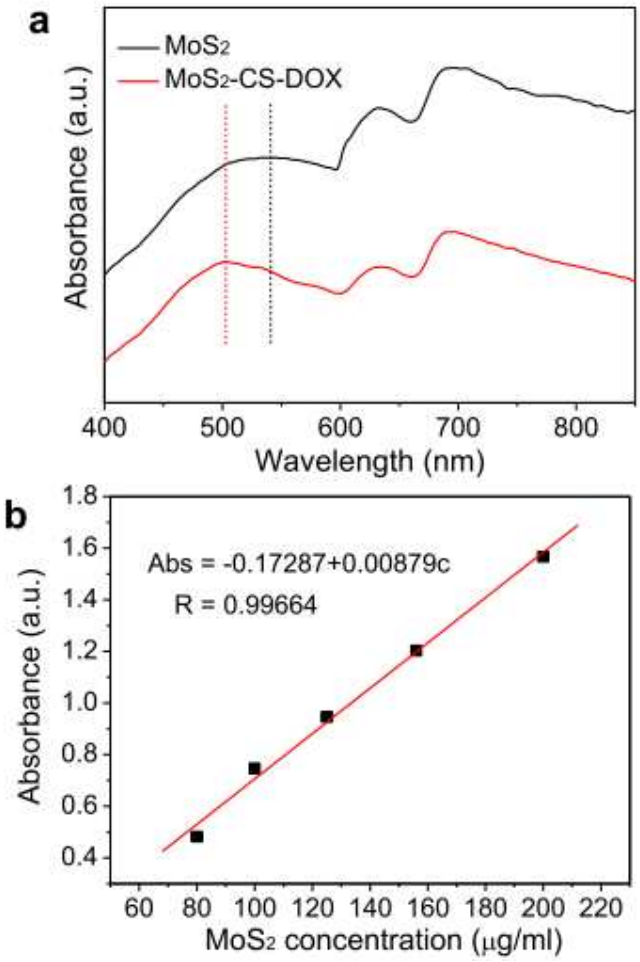

Figure S6. (a) UV-vis absorbance spectra of MoS_2-CS and MoS_2-CS-DOX. DOX loaded on MoS_2-CS was evidenced by an additional absorption peak centered at ~500 nm. (b) Plots of linear fitting extinction *versus* wavelength for MoS_2-CS aqueous solution with various concentrations at 691 nm, which was used to determine the concentration of the unknown MoS_2-CS aqueous dispersions.

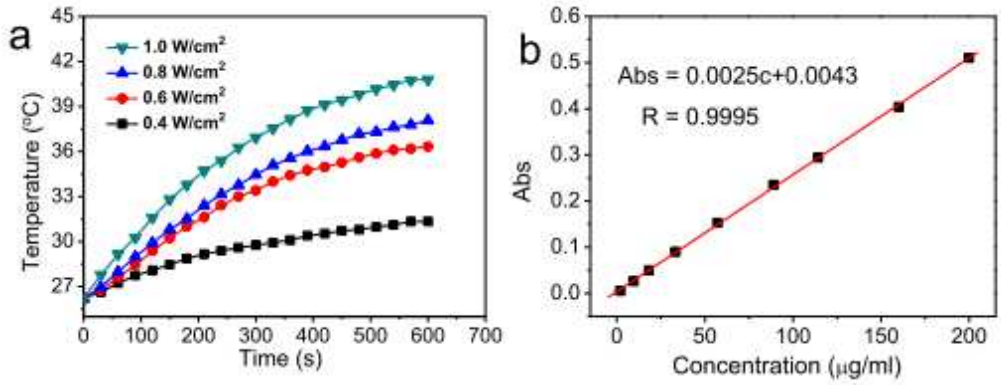

Figure S7. (a) The temperature elevation of MoS_2-CS aqueous solution (100 μg/ml) irradiated by 808-nm laser with different power density *versus* a function of irradiation time (0-10 min). These results suggested that the temperature gradually increased with the increase of power densities, showing a power-dependent manner. (b) Plots of linear fitting extinction *versus* wavelength for MoS_2-CS in aqueous solution with various concentrations at absorption peak of 808 nm.

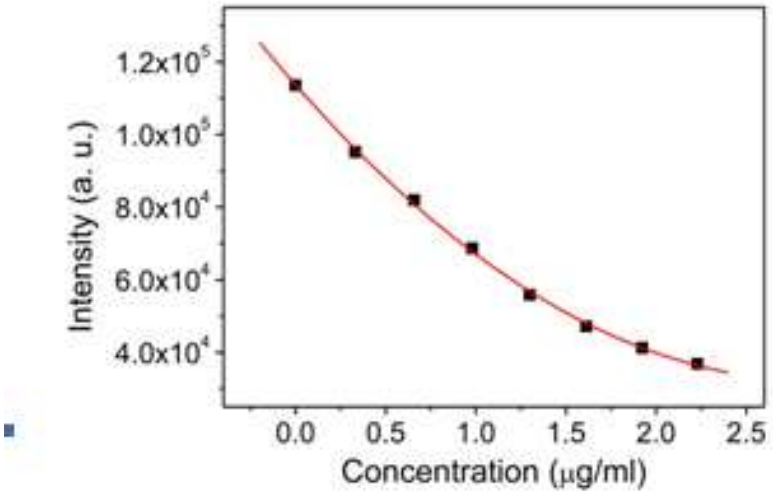

Figure S8. A quenching of the fluorescence when the DOX is linked at the MoS_2-CS with respect to the free DOX.

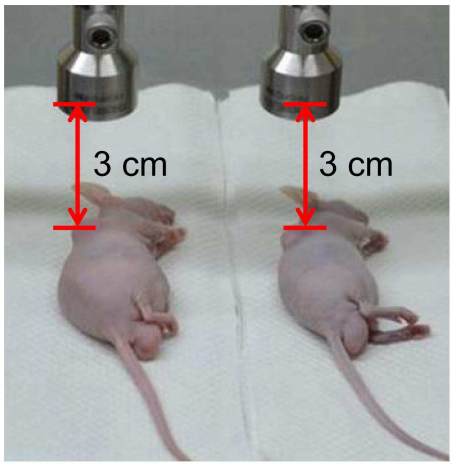

Figure S9. Photothermal therapy setup showing laser and the Panc-1-bearing mice.

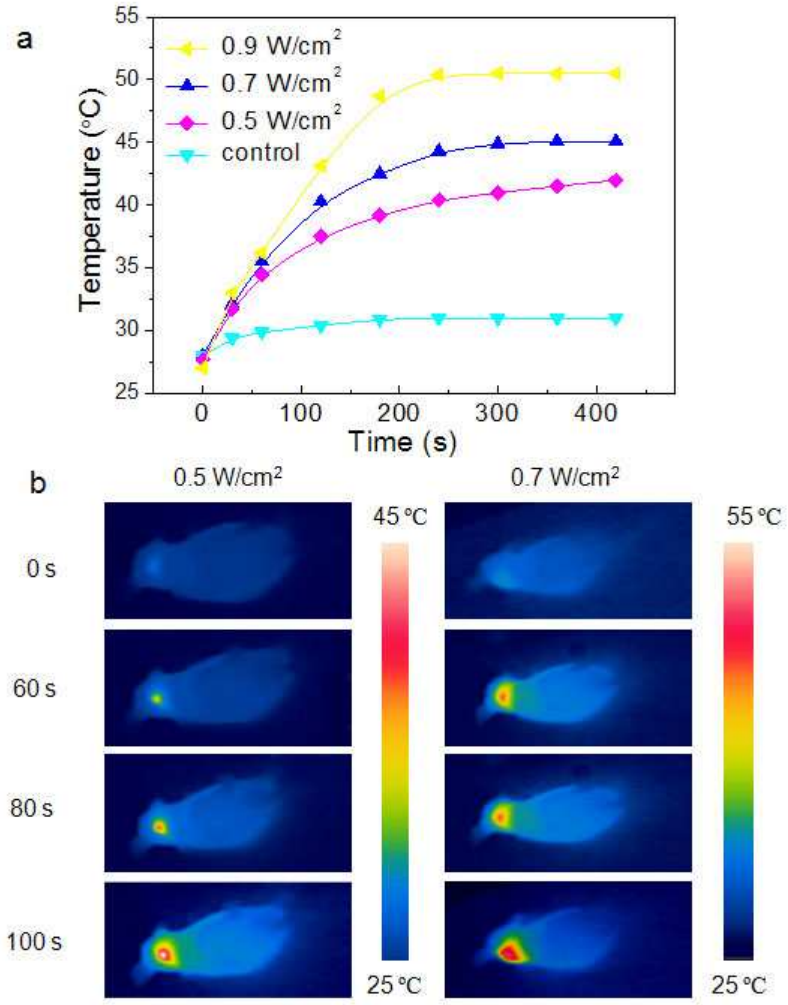

Figure S10. (a) The temperature changes on tumors of mice under different treatments. (b)Infrared thermal images of Panc-1 tumor-bearing mice injected with MoS_2-CS-DOXwhich were exposed to an 808 nm laser at different output power densities.

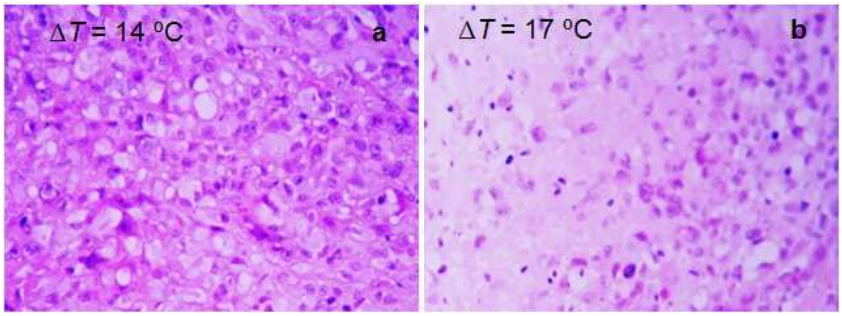

Figure S11. Histological images of tumors collected from the groups of MoS_2-CS-DOX+NIR 808-nm laser with different power densities.