Supplementary Material for

Redox chemistry-enabled stepwise surface dual nanoparticle engineering of 2D MXenes for tumor-sensitive T_1 and T_2 MRI-guided photonic breast-cancer hyperthermia in the NIR-II biowindow

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CONTENTS

Part A. Supplementary experimental details

1. Calculation of Photothermal conversion efficiency

To assess the NIR absorption capability of Fe_3O_4/MnO_x-Nb_2C-SP composite nanosheets, the extinction coefficient α of those composite nanosheets is obtained, according to the Lambert-Beer law:

$$A\ (\lambda)\ L = \alpha LC \qquad (1)$$

Where A is the absorbance at a wavelength (λ), α is the extinction coefficient, L is path-length (1 cm), and C is the molar concentration of the Fe_3O_4/MnO_x-Nb_2C-SP composite nanosheets (g L^{-1}). The extinction coefficient (α) is given by plotting the slope (L g^{-1} cm^{-1}) of each linear fit against wavelength. The extinction coefficient (α) of Fe_3O_4/MnO_x-Nb_2C-SP composite nanosheets can be determined to be 2.50 L g^{-1} cm^{-1} (**Figure 4a**).

According to previous report,[1] the total energy balance for the whole system is

$$\sum_i m_i C_{p,i}\frac{dT}{dt} = Q_{Fe3O4/MnOx-Nb2C-SP} + Q_{Dis} - Q_{surr} \qquad (2)$$

where m and C_p are the mass and heat capacity of solvent and T is the solution temperature, $Q_{Fe3O4/MnOx-Nb2C-SP}$ represents the photothermal energy inputted by Fe_3O_4/MnO_x-Nb_2C-SP nanocomposites. Q_{Dis} means the baseline energy inputted by the sample cell and Q_{surr} is the heat conduction away from the system surface by atmosphere.

$Q_{Fe3O4/MnOx-Nb2C-SP}$ is heat dissipated by electron-phonon relaxation of plasmons on the Fe_3O_4/MnO_x-Nb_2C-SP nanocomposites surface induced by 1064 nm laser irradiation of those nanocomposites at a resonant wavelength λ.

$$Q_{Fe3O4/MnOx-Nb2C-SP} = I\left(1 - 10^{-A_{1064}}\right)\eta \tag{3}$$

where I express the incident laser power (mW), A_{1064} represents the absorbance of the Fe_3O_4/MnO_x-Nb_2C-SP at wavelength of 1064 nm, and η is the photothermal transduction efficiency. Q_{Dis} means heat dissipated from light absorbed by the sample cell, and it was calculated independently to be $Q_{Dis} = (5.40 \times 10^{-4})I$ (mW) using a sample cell containing pure water without nanoparticles. Q_{surr} represents nearly proportional to the linear thermal driving force in this system, with a heat-transfer coefficient, h, is the proportionality constant.

$$Q_{surr} = hS(T - T_{surr}) \tag{4}$$

where S represents the surface area of the container, and T_{surr} expresses the ambient surrounding temperature.

To acquire the hS, a dimensionless driving force temperature, θ, is introduced, using the maximum system temperature (T_{max}).

$$\theta = \frac{T - T_{surr}}{T_{max} - T_{surr}} \tag{5}$$

and a sample system time constant τ_s.

$$\tau_s = \frac{\sum_i m_i C_{p,i}}{hS} \tag{6}$$

which is substituted into equation (2) to

$$\frac{d\theta}{dt}=\frac{1}{\tau_s}\left[\frac{Q_{Fe3O4/MnOx-Nb2C-SP}+Q_{Dis}}{hS(T_{max}-T_{surr})}-\theta\right] \quad (7)$$

When turning off the laser source, $Q_{Fe3O4/MnOx-Nb2C-SP}+Q_{Dis}=0$, rearranging equation (7) to

$$t=-\tau_s \ln\theta \quad (8)$$

Hence, τ_s was determined to be 170.00 s from the data in **Figure 4e**. In addition, the *m* is 0.10 g and the *C* is 4.20 J g^{-1}. According to equation (6), the *hS* is calculated to be 2.47 mW °C^{-1}.

During laser irradiation, $Q_{Fe3O4/MnOx-Nb2C-SP}+Q_{Dis}$ is finite, and the external heat (Q_{surr}) is increased along with the rise of the temperature according to the equation (4), the system temperature will reach to a maximum value when output heat equals to input heat

$$Q_{Fe3O4/MnOx-Nb2C-SP}+Q_{Dis}=hS(T_{max}-T_{surr}) \quad (9)$$

where T_{max} means the equilibrium temperature. The 1064 nm laser photothermal conversion efficiency (η) can be calculated by equation (3) for $Q_{Fe3O4/MnOx-Nb2C-SP}$ into equation (9) and reducing to obtain

$$\eta=\frac{hS(T_{max}-T_{surr})-Q_{Dis}}{I(1-10^{-A_{1064}})} \quad (10)$$

where the $(T_{max}-T_{surr})$ was 42.9 °C according to **Figure 4e**, *I* is 500 mW, Q_{Dis} was measured independently to be 0.27 mW, A_{1064} is the absorbance of Fe_3O_4/MnO_x-Nb_2C-SP at 1064 nm (**Figure 4a**). Putting these values into equation (10), the 1064 nm laser photothermal conversion efficiency (η) of Fe_3O_4/MnO_x-Nb_2C-SP can be calculated to be 30.9%.

2. *In vivo* toxicity experiment

The biosafety of the Fe_3O_4/MnO_x-Nb_2C-SP composite nanosheets was verified by blood routine testing, including the indexes of alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN), creatinine (CR), hemoglobin (Hb), hematocrit (HCT), lymphocytes (LYM), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), mean corpuscular volume (MCV), platelets (PLT), red blood cells (RBC) and white blood cells (WBC).

Part B. Supplementary figures and distinctions

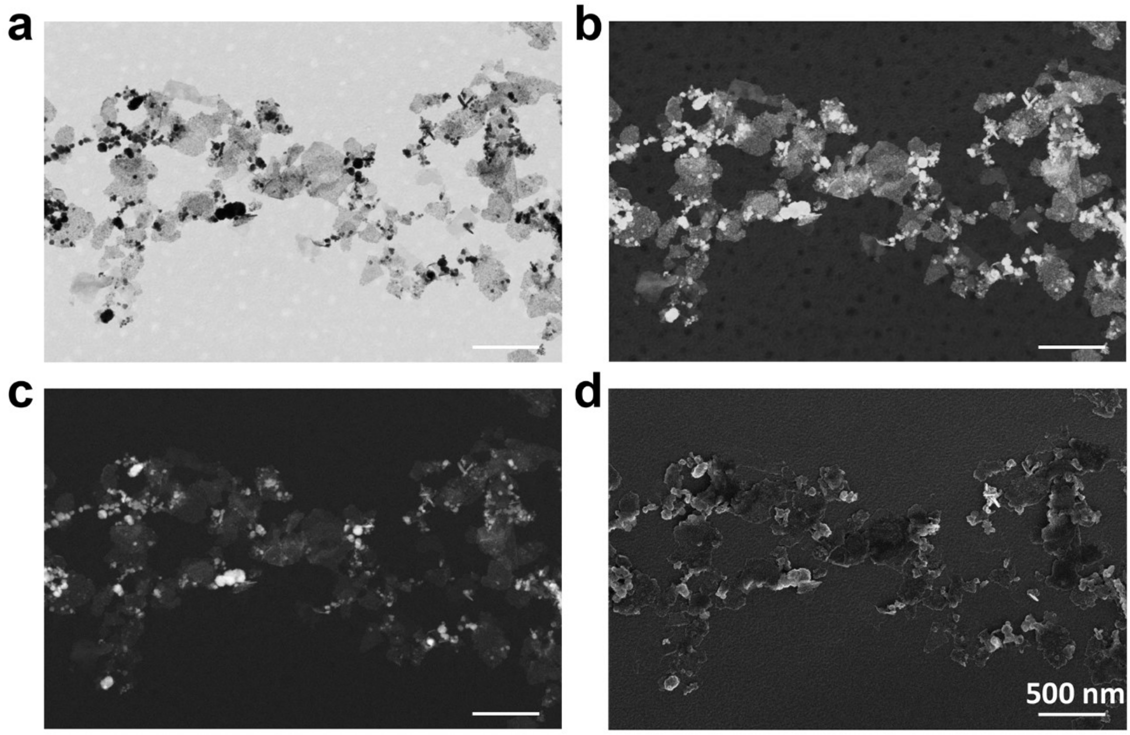

Figure S1. (a) Bright-field STEM, (b) dark-field STEM, (c) high-Angle Annular Dark Field (HAADF)-STEM and (d) SEM images of Fe_3O_4/MnO_x-Nb_2C composite MXene nanosheets.

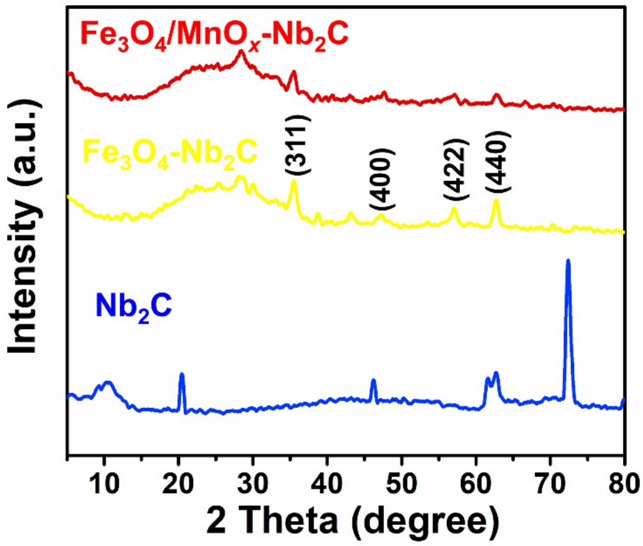

Figure S2. X-ray diffraction (XRD) of Nb_2C, Fe_3O_4-Nb_2C and Fe_3O_4/MnO_x-Nb_2C composite nanosheets.

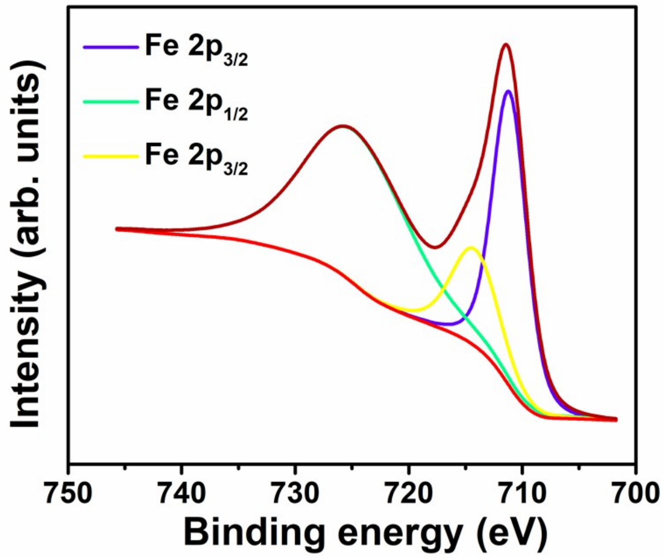

Figure S3. X-ray photoelectron spectroscopy (XPS) spectra of Fe 2p peaks of Fe_3O_4/MnO_x-Nb_2C composite nanosheets.

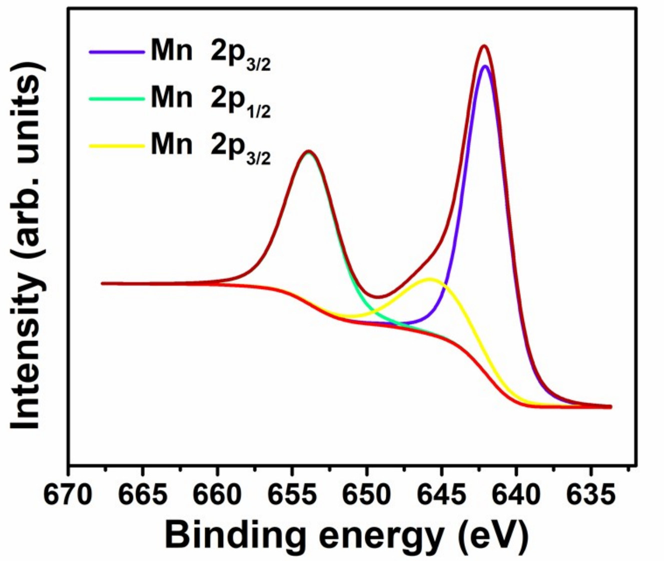

Figure S4. X-ray photoelectron spectroscopy (XPS) spectra of Mn 2p peaks of Fe_3O_4/MnO_x-Nb_2C composite nanosheets.

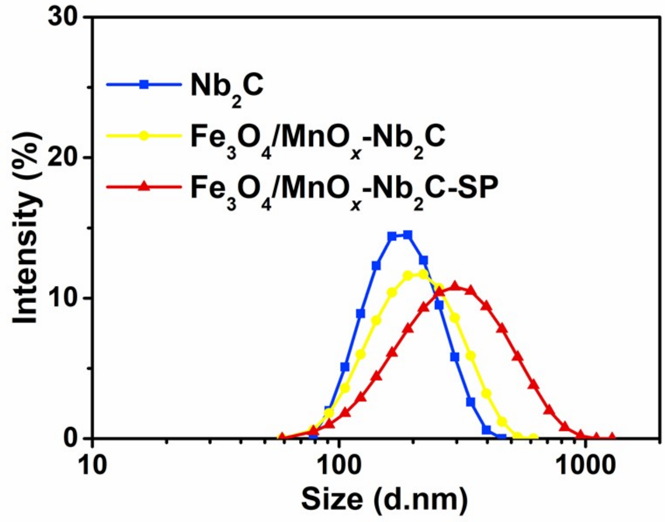

Figure S5. Dynamic light scattering (DLS) curves of Nb_2C nanosheets, Fe_3O_4/MnO_x-Nb_2C and Fe_3O_4/MnO_x-Nb_2C-SP composite nanosheets in aqueous solution.

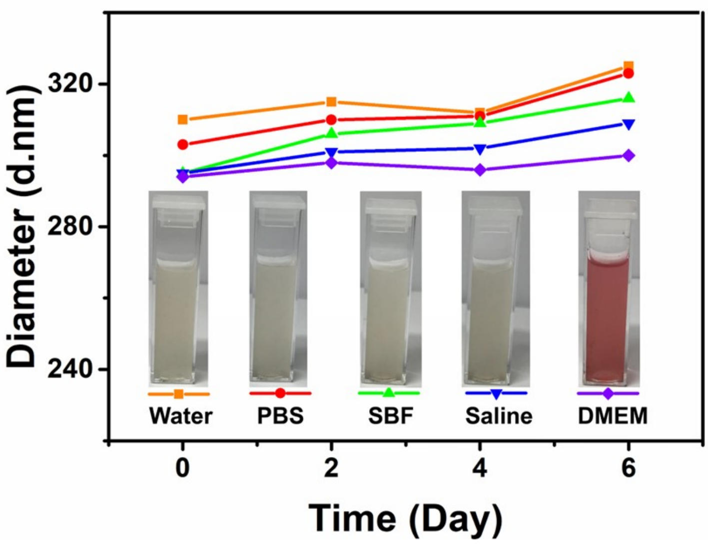

Figure S6. Diameter changes of Fe_3O_4/MnO_x-Nb_2C-SP composite nanosheets in various solutions (water, PBS, SBF, saline, and DMEM) at given time points (Inset: the corresponding photographic images at the 6^{th} day).

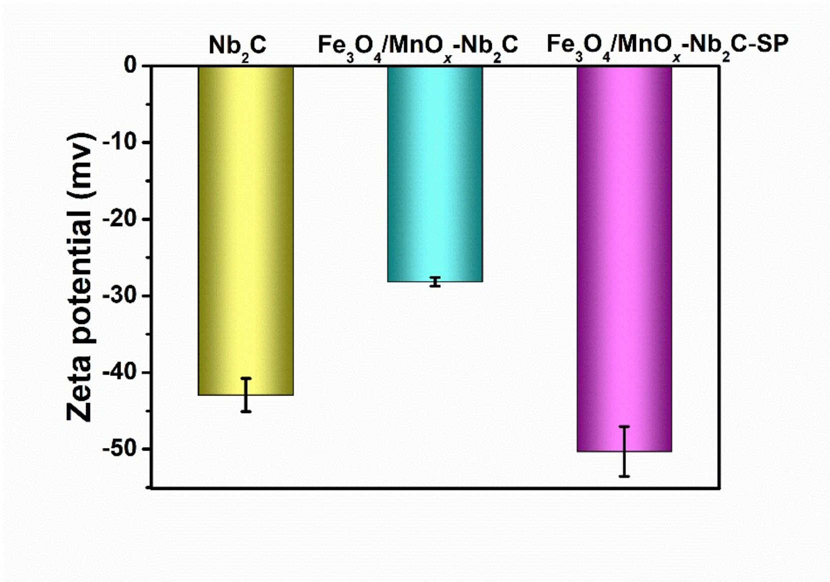

Figure S7. Zeta potential of Nb_2C nanosheets, Fe_3O_4/MnO_x-Nb_2C and Fe_3O_4/MnO_x-Nb_2C-SP composite nanosheets in aqueous solution.

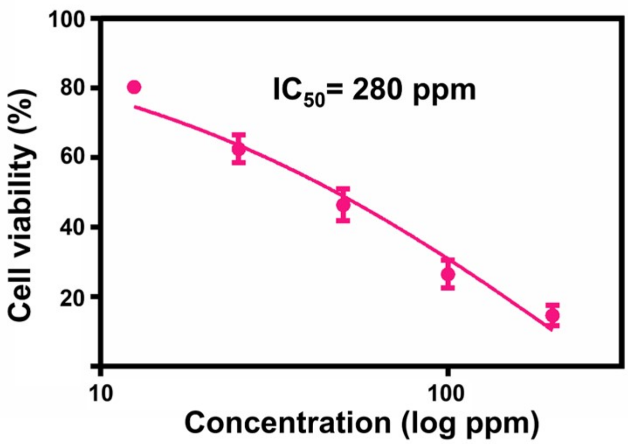

Figure S8. Half maximal inhibitory concentration (IC_{50}) value of Fe_3O_4/MnO_x-Nb_2C-SP composite nanosheets under the NIR irradiation as calculated to be 280 ppm.

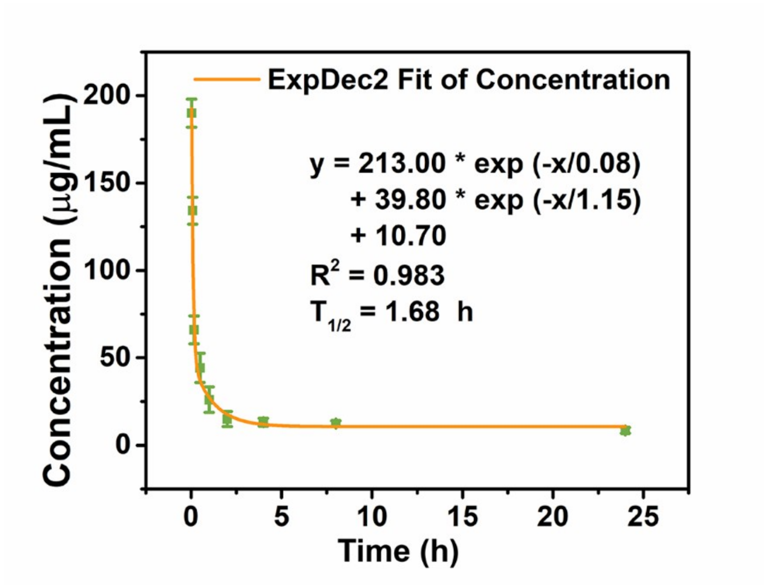

Figure S9. Blood circulation curve of Fe_3O_4/MnO_x-Nb_2C-SP by measuring the Nb concentration in blood of health Kunming mice at varied time intervals. The half-time ($T_{1/2}$) was calculated to be 1.68 h..

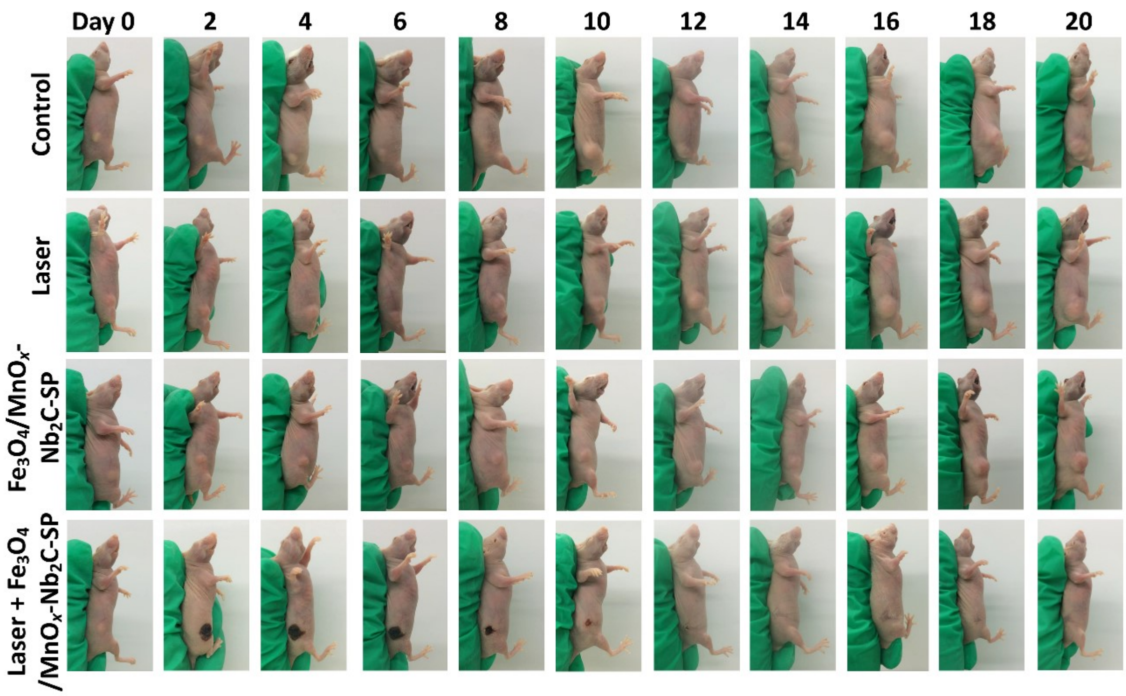

Figure S10. Digital photography of 4T1 tumor-bearing BALB/c nude mice in different treatment groups within 20 days.

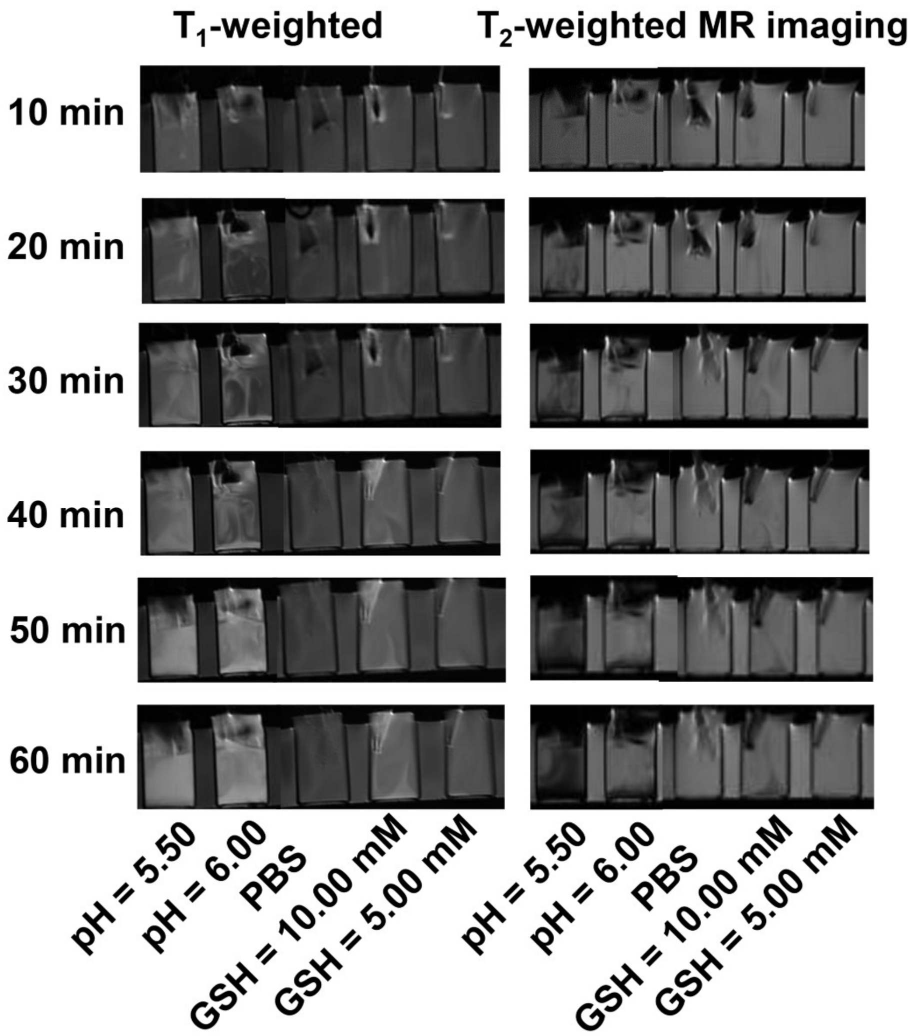

Figure S11. *In vitro* dynamic measurement of T_1&T_2-weighted MR imaging of Fe_3O_4/MnO_x-Nb_2C-SP in the buffer solution with different pH values and GSH concentration (pH = 5.50, 6.00, GSH = 5.00, 10.00 mM) and PBS.

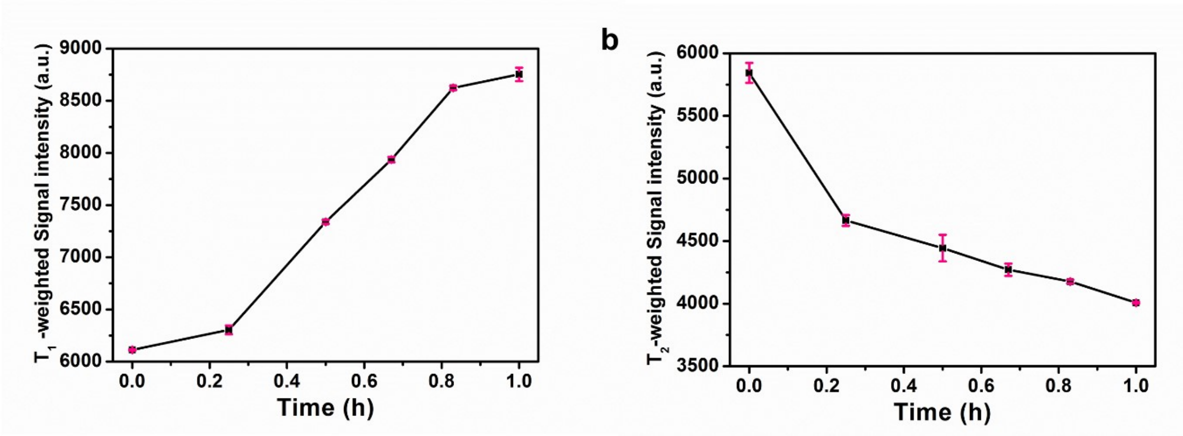

Figure S12. (a) T_1-weighted and (b) T_2-weighted MRI-signal intensities of tumor site with the prolonging of duration after the intravenous administration of Fe_3O_4/MnO_x-Nb_2C-SP at given time points.

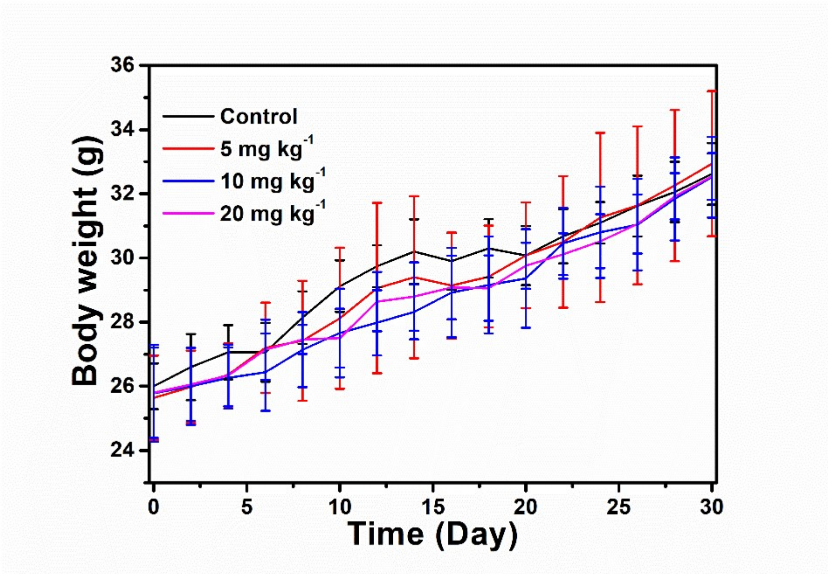

Figure S13. Time-dependent body-weight changing profiles of Kunming mice within 30 days after intravenous administration of Fe_3O_4/MnO_x-Nb_2C-SP at elevated doses (0, 5, 10 and 20 mg kg^{-1}).

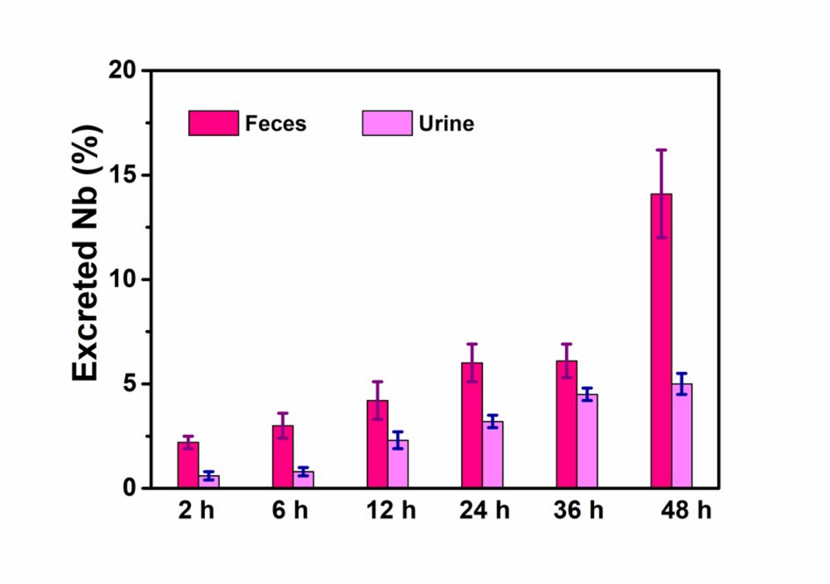

Figure S14. Accumulated (feces and urine) Ta excretion out of the health Kunming mice after the intravenous administration of Fe_3O_4/MnO_x-Nb_2C-SP for different durations.

Part C. References

1. D. K. Roper, W. Ahn and M. Hoepfner, *J Phys Chem C Nanomater Interfaces*, 2007, **111**, 3636-3641.