Electronic Supplementary Material (ESI) for Biomaterials Science.

Supporting Information

Mitochondria-Targeted Zirconium Metal-Organic Frameworks for Enhancing Microwave Thermal Therapy Against Tumor

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Calculation of the MW-thermo conversion efficiency

The MW-thermo conversion efficiency was calculated according to our previous work as follows:

Firstly, based on conservation of energy for the system:

$$Q_{input} \cdot \eta = Q_{output} = Q_{heat} + Q_{loss} \quad (1)$$

$$Q_{input} = p \cdot s_0 \cdot (t_n - t_0) \quad (2)$$

$$Q_{heat} = \sum_{t=t_0}^{t=t_n} C_{solution} \cdot m \cdot \Delta T = C_{solution} \cdot m \cdot (T_1 - T_0) + C_{solution} \cdot m \cdot (T_2 - T_1) + \ldots + C_{sol} \ldots) + C_{solution} \cdot m \cdot (T_n - T_{n-1}) = C_{solution} \cdot m \cdot (T_n - T_0) \quad (3)$$

Assumption ①: $T_{Env} \equiv T_0$ (4)

$$Q_{loss} = \sum_{t=t_0'}^{t=t_n'} u \cdot s_0 \cdot \Delta(T_{ZrMOF} - T_{Env}) \cdot \Delta t = \sum_{t=t_0'}^{t=t_n'} u \cdot s_0 \cdot \Delta(f_1(t) - f_2(t)) \cdot \Delta t \quad (5)$$

Assumption ② $:\lim \Delta t = \lim(t_n - t_{n-1}) = dt \to 0^+$ (6)

$$\Delta(f_1(t) - f_2(t)) \cdot \Delta t = \sum_{t=t_0}^{t=t_n} [f_1(t) - f_2(t)]dt = \int_{t_0}^{t_n} [f_1(t) - f_2(t)]dt = \Delta S \quad (7)$$

$$Q_{loss} = u \cdot s_0 \cdot \Delta S \quad (8)$$

Then $u \cdot s_0$ was calculated as follows:

$$\sum_{t=t_0'}^{t=t_n'} C_{solution} \cdot m \cdot \frac{dT}{dt} = -u \cdot s_0 \cdot \Delta T \quad (9)$$

$$\theta \ was \ introduced: \theta = \frac{\Delta T}{T_{max}} \quad (10)$$

$$\sum_{t=t_0'}^{t=t_n'} C_{solution} \cdot m \cdot \frac{d\theta}{dt} = -u \cdot s_0 \cdot \theta \quad (11)$$

$$dt = -\frac{\sum_{t=t_0'}^{t=t_n'} C_{solution} \cdot m}{u \cdot s_0} \cdot \frac{d\theta}{\theta} \quad (12)$$

$$\xi \ was \ introduced: \xi = \frac{\sum_{t=t_0'}^{t=t_n'} C_{solution} \cdot m}{u \cdot s_0} \quad (13)$$

$$t = \xi \cdot (-ln\theta) + a \quad (14)$$

Finally, MW-thermo conversion efficiency (η) of ZrMOF NCs was calculated by the following equation:

$$\eta = \frac{\left[\sum_{t=t_0}^{t=t_n} C_{solution} \cdot m \cdot \Delta T + Q_{loss}\right]}{Q_{input}} = \Bigg[C_{solution} \cdot m \cdot (T_n - T_0) + \frac{\sum_{t=t_0'}^{t=t_n'} C_{solution} \cdot m}{\xi_s} \cdot \int_{t_0}^{t_n} [f_1$$

$$(t_n - t_0)$$

m (g): Total mass of the solution and ZrMOF NCs
ΔT (K): Temperature change of the system
Q_{input} (J): Electromagnetic energy of MW radiation
Q_{heat} (J): Thermal energy of the solution containing ZrMOF NCs
Q_{loss} (J): Lost of Thermal energy to the surroundings
η : MW-thermo conversion efficiency of ZrMOF NCs
P (W/cm^2): Power of MW irradiation
S_0 (cm^2): Heating surface area of the container
T_0 (K): Initial temperature before MW irradiation
T_n (K): Highest temperature of the steady state
u (W/(m•K)): Heat transfer coefficient of the natural convection
T_{ZrMOF} (K): Temperature of the solution containing ZrMOF NCs
T_{Env} (K): Ambient surrounding temperature
$f_1(t)$ and $f_2(t)$: Function formula of T_{ZrMOF} and T_{Env} for time

Table S1. Parameters for calculating MW-thermo conversion efficiency η of ZrMOF NCs dispersed in three solutions (water, 0.9 wt.% NaCl solution and DMEM).

$Sample$	$\sum c \cdot m \cdot \Delta T$ **(J)**	ξ_s	Q_{loss} (J)	Q_{input} (J)	η (%)
Water	3.73	445.36	65.04	2165.11	3.2 ±0.4
NaCl	61.82	88.67	437.90	2165.11	23.1 ± 0.9
DMEM	87.30	70.13	553.59	2165.11	29.6 ± 0.7
ZrMOF in Water	5.49	427.14	71.69	2165.11	3.6 ± 0.6
ZrMOF in NaCl	90.74	72.45	529.30	2165.11	28.6 ± 0.9
ZrMOF in	113.17	65.79	679.80	2165.11	36.6 ± 0.9

DMEM

DOX loading and pH-controled release test

Standard calibration curve (the correlation coefficient was 0.99821) was as follows:

$y = 0.05531 + 0.02045 \times x$

y represents the absorption intensity of DOX at the wavelength of 483 nm, and *x* represents the corresponding concentration of DOX (μg/mL). And the loading rate of DOX-loaded ZrMOF-PEG-TPP ($R_{loading}$), the encapsulation efficiency of DOX ($R_{encapsulation}$) and the release rate of DOX-loaded ZrMOF-PEG-TPP ($R_{release}$) were calculated as follows, respectively:

$$R_{loading} = \frac{m_{DOX}^{'}}{m_{ZrMOF-PEG-TPP} + m_{DOX}^{'}} \quad (1)$$

$$R_{encapsulation} = \frac{m_{DOX}^{'}}{m_{DOX}^{0}} \quad (2)$$

$$R_{release} = \frac{m_{DOX}^{''}}{m_{DOX}^{'}} \quad (3)$$

$m_{ZrMOF-PEG-TPP}$ represents the amount of ZrMOF-PEG-TPP NCs; m_{DOX}^{0} was amount of DOX added in ZrMOF-PEG-TPP@DOX;$m_{DOX}^{'}$ and $m_{DOX}^{''}$ representloading capacity and release amount of DOX on ZrMOF-PEG-TPP@DOX NCs, respectively.

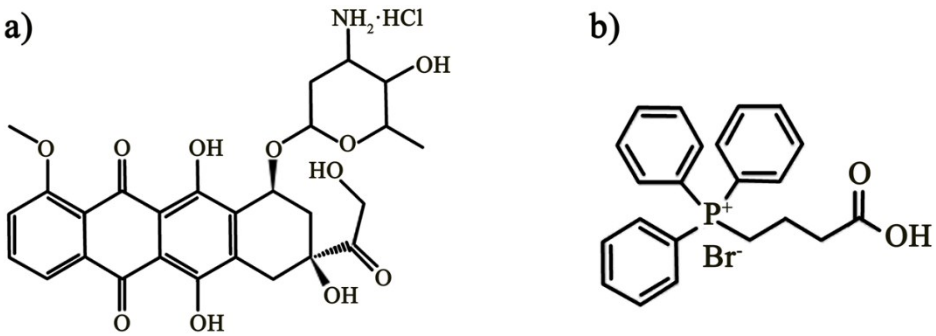

Fig. S1 The molecular structures of a) doxorubicin hydrochloride (DOX) and b) 3-Carboxypropyl triphenylphosphonium bromide (TPP).

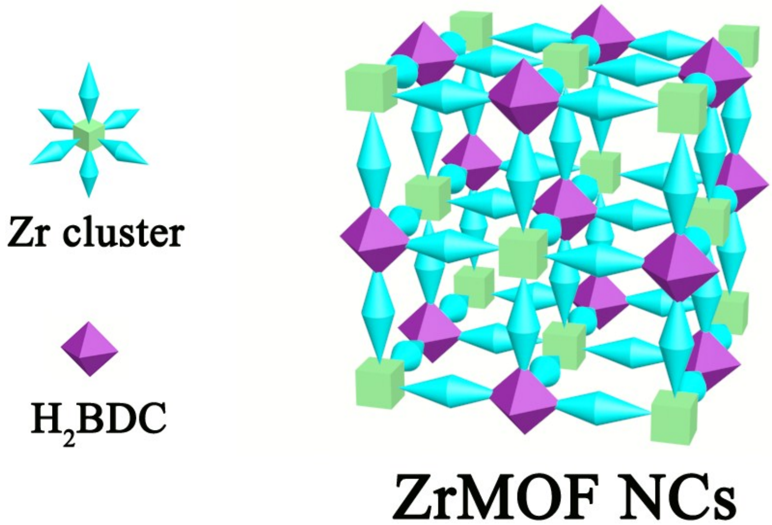

Fig. S2 The crystal structure of ZrMOF NCs. Zr cluster represents the inner $Zr_6O_4(OH)_4$ core of ZrMOF NCs.

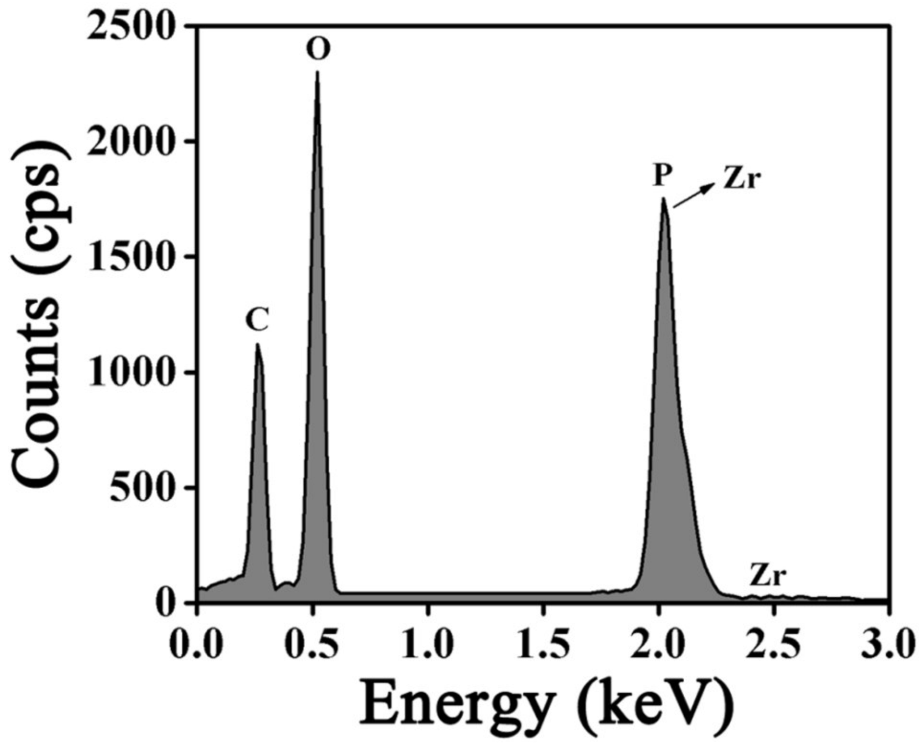

Fig. S3 Energy dispersive spectrum of ZrMOF-PEG-TPP NCs.

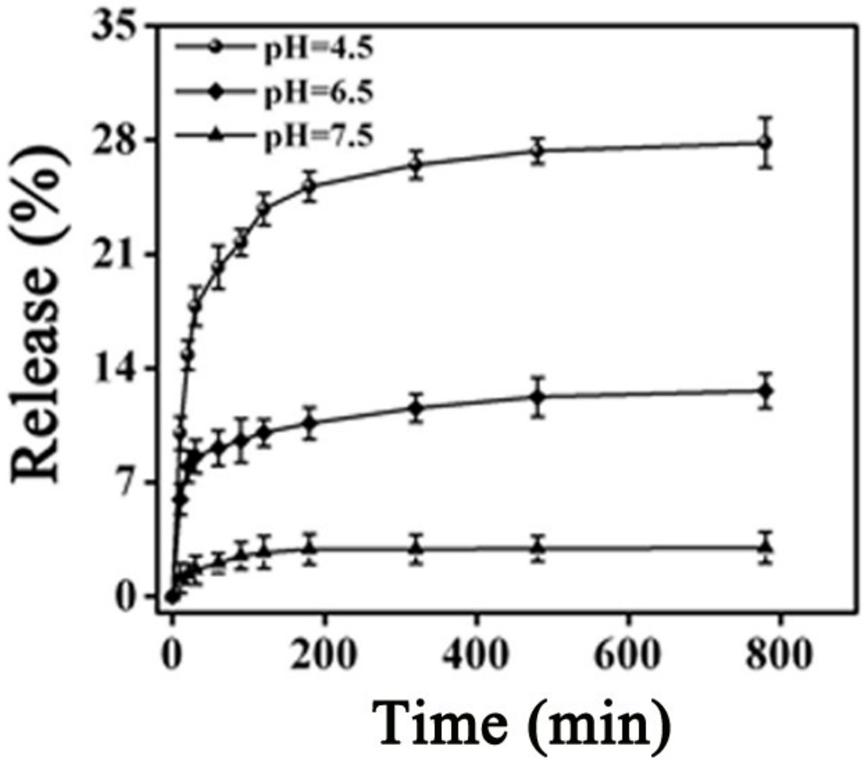

Fig. S4 pH-controled release curves of ZrMOF-PEG-TPP@DOX NCs in different pH of PBS with time.

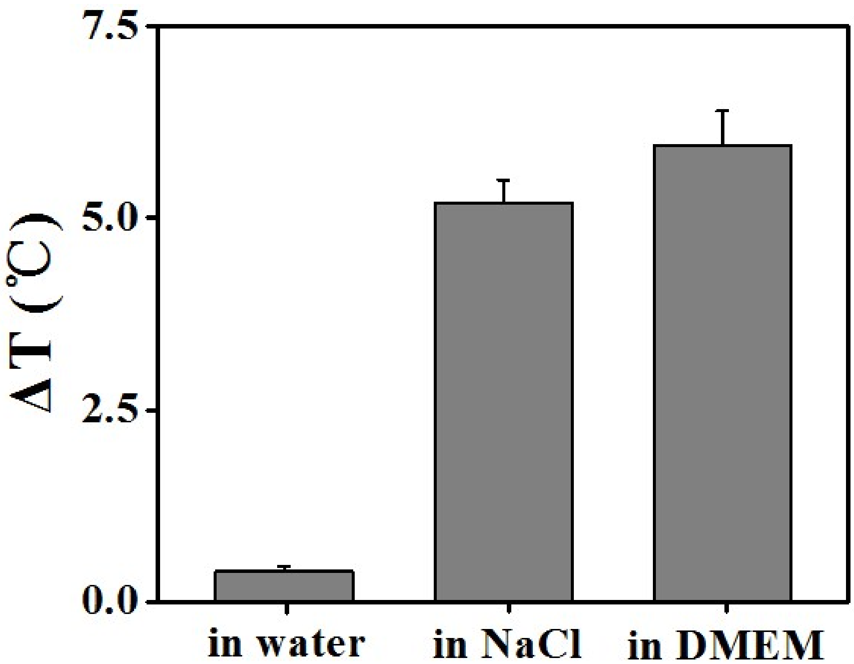

Fig. S5 The temperature change between water, 0.9 wt. % NaCl solution, DMEM and ZrMOF NCs dispersed in water, 0.9 wt. % NaCl solution and DMEM (10 mg/mL, 1.8 W/cm^2, 5 min), respectively.

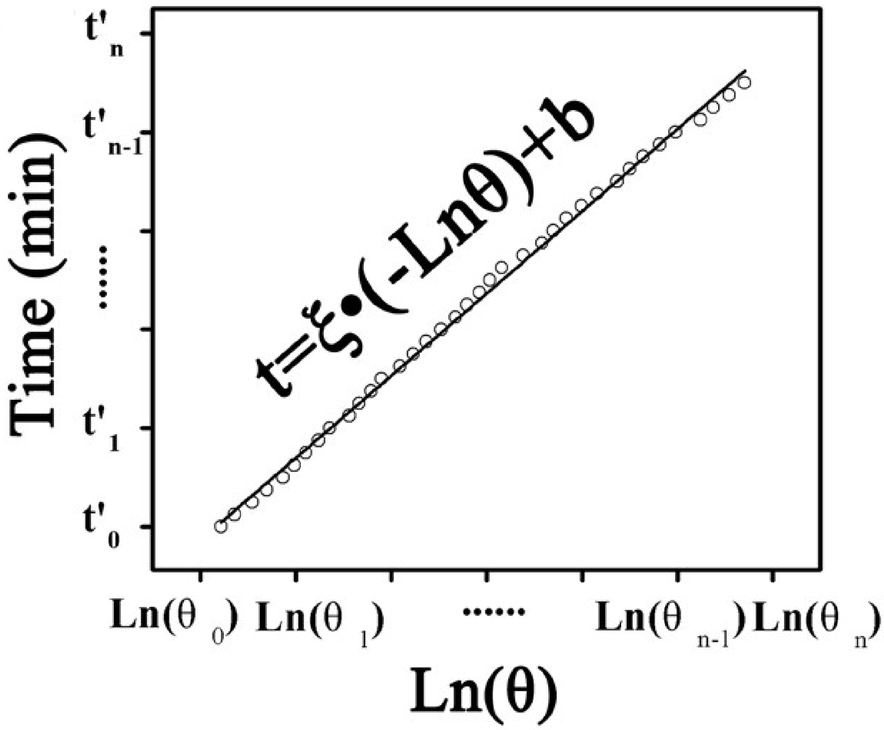

Fig. S6 The linear fitting of cooling curve for ZrMOF NCs accordingly.

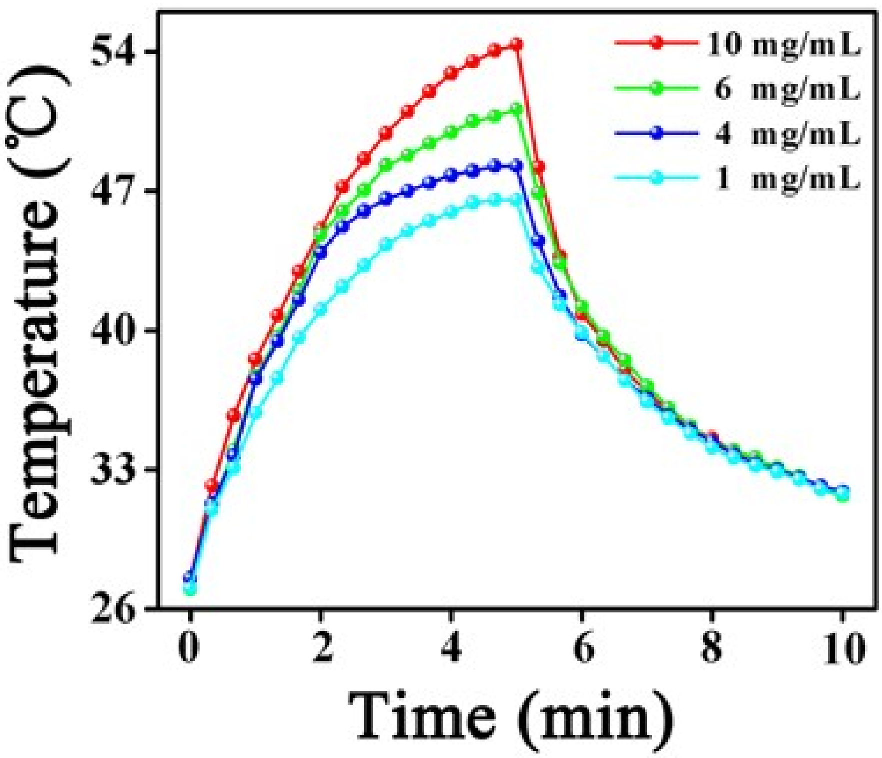

Fig. S7 At different concentrations of ZrMOF NCs (1.8 W/cm^2), the heating curves of ZrMOF NCs dispersed in DMEM under MW irradiation (5 min).

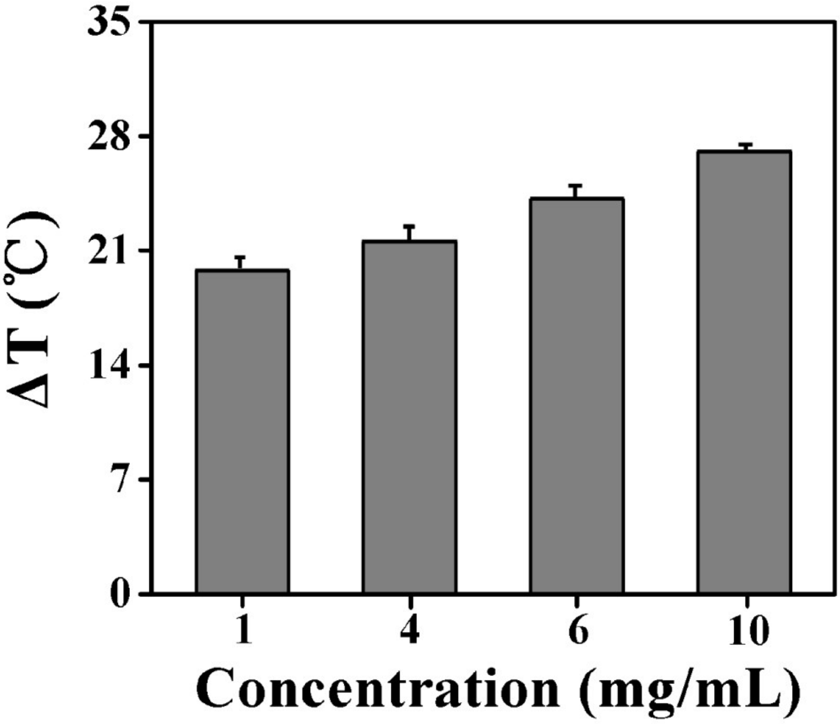

Fig. S8 The temperature changes of ZrMOF NCs dispersed in DMEM at the concentration of 1, 4, 6 and 10 mg/mL (1.8 W/cm^2, 5min).

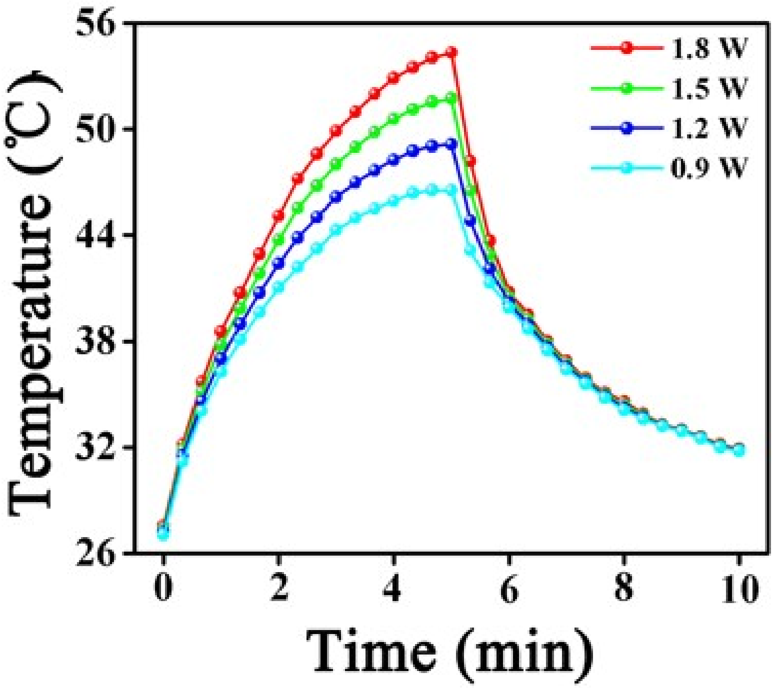

Fig. S9 At different MW irradiation powers of ZrMOF NCs (10 mg/mL), the heating curves of ZrMOF NCs dispersed in DMEM under MW irradiation (5 min).

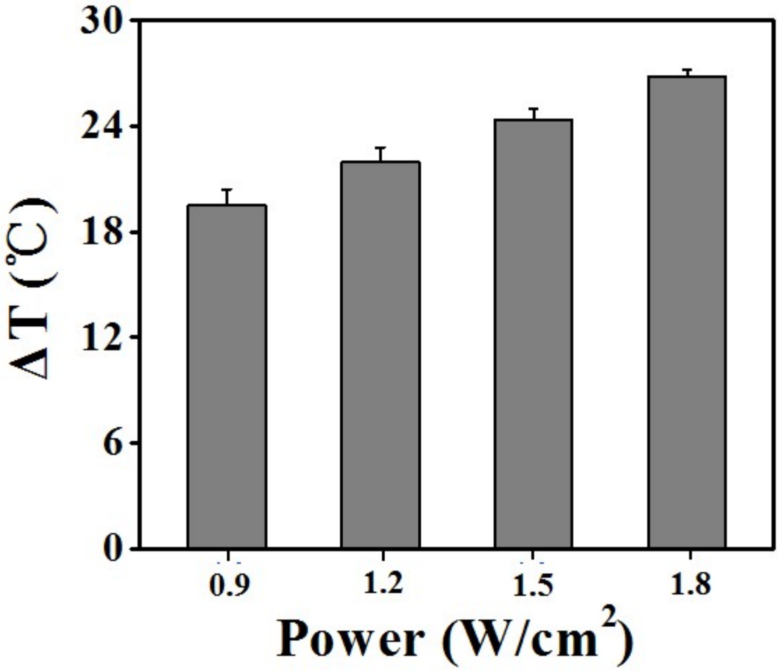

Fig. S10 The temperature changes of ZrMOF NCs dispersed in DMEM at the MW irradiation power of 0.9, 1.2, 1.5 and 1.8 W/cm^2 (10 mg/mL, 5 min).

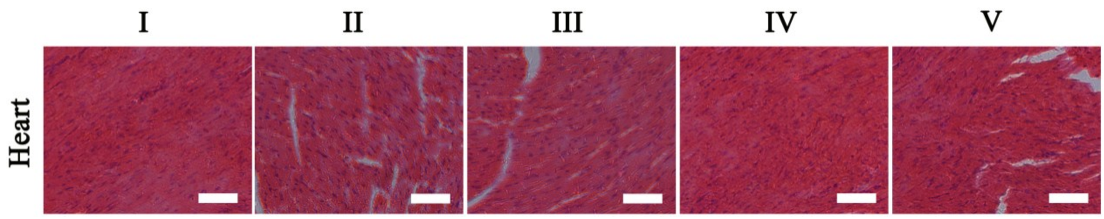

Fig. S11 H&E stained images of the heart in the mice with different treatments. I, II, III, IV and V was 5 wt.% glucose solution, MW, ZrMOF-PEG-TPP@DOX NCs, ZrMOF-PEG@DOX NCs + MW and ZrMOF-PEG-TPP@DOX NCs + MW groups, respectively. And the scale bar was 25 μm.

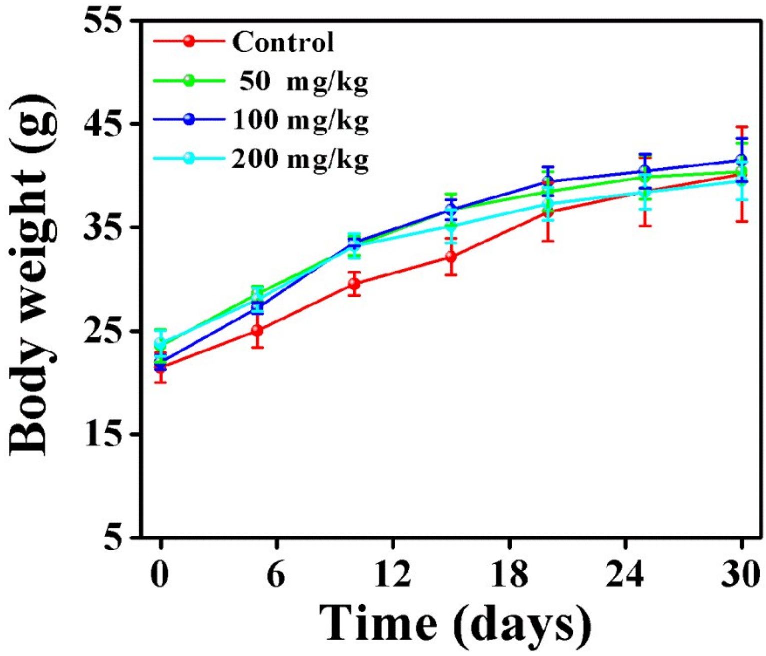

Fig. S12 The body weight changes of normal mice intravenously injected with ZrMOF-PEG-TPP@DOX NCs at the concentrations of 50, 100 and 200 mg/kg.

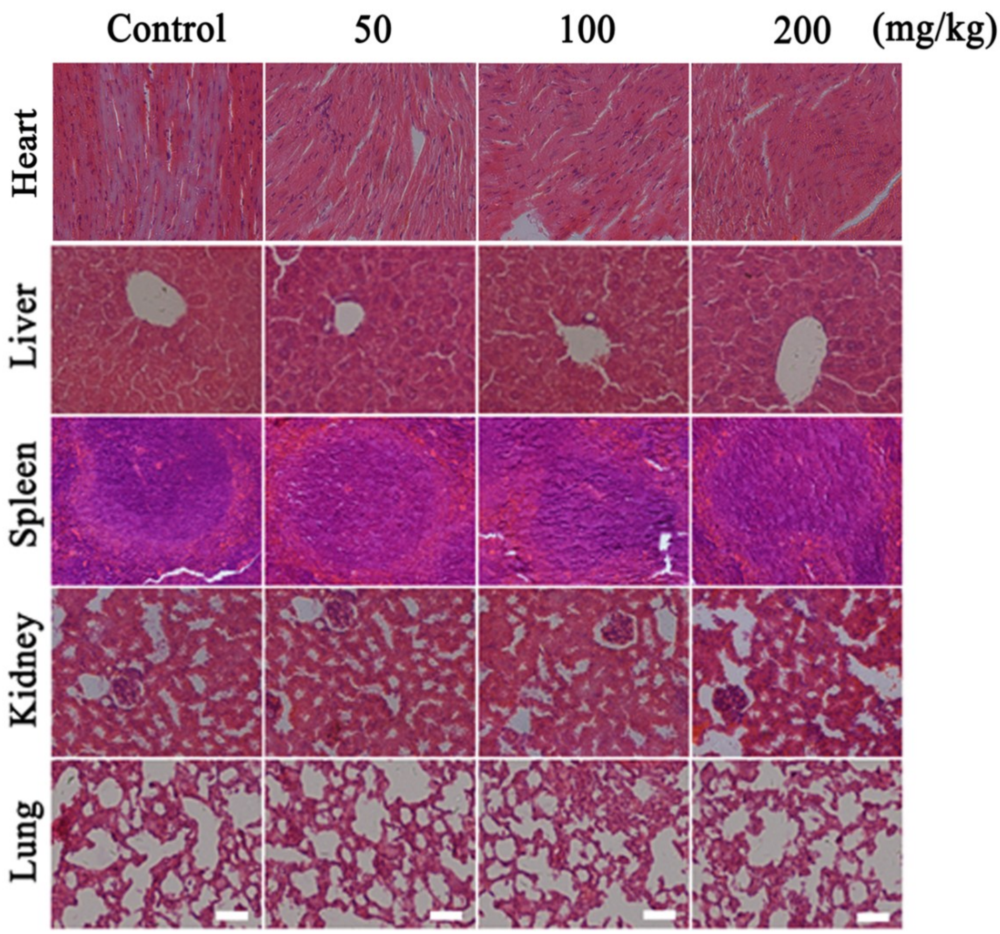

Fig. S13 H&E stained images of normal mice intravenously injected with ZrMOF-PEG-TPP@DOX NCs at the concentrations of 50, 100 and 200 mg/kg. And the scale bar was 25 μm.