Supporting Information

A Biocompatible Metal-Organic Framework as a pH and Temperature Dual-responsive Drug Carrier

Wenxin Lin,*[a] Yuanjing Cui,[b] Yu Yang, [b] Quan Hu[c] and Guodong Qian*[b]

[a] Department of Materials Engineering, College of Materials and Textile, Zhejiang Sci-Tech University, Hangzhou 310018, PR China

[b] State Key Laboratory of Silicon Materials, Cyrus Tang Center for Sensor Materials and Applications, School of Materials Science & Engineering, Zhejiang University, Hangzhou 310027, PR China

[c]Department of Pharmacy, School of Medicine, Hangzhou Normal University, Hangzhou 310036, PR China

* Corresponding Authors

E-mail: linwx@zstu.edu.cn (W. Lin), gdqian@zju.edu.cn (G. Qian)

Table S1. Crystal data and structure refinement for Zn-GA.

Compound	Zn-GA	
CCDC no.	1501246	
Empirical formula	$C_5H_{11}NO_6Zn$	
Formula weight	246.52	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P 2_1 2_1 2_1	
Unit cell dimensions	a = 7.2283(4) Å	□= 90°.
	b = 10.4670(4) Å	□= 90°.
	c = 11.1858(7) Å	□ = 90°.
Volume	846.30(8) $Å^3$	
Z	4	
Density (calculated)	1.935 Mg/m^3	
Absorption coefficient	2.902 mm^{-1}	
F(000)	504	
Theta range for data collection	2.665 to 26.095°.	
Index ranges	-8<=h<=8, -12<=k<=12, -13<=l<=13	
Reflections collected	8907	

Independent reflections	1666 [R(int) = 0.0252]
Completeness to theta = 25.242°	99.9 %
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1666 / 0 / 127
Goodness-of-fit on F^2	1.011
Final R indices [I>2sigma(I)]	R_1[a] = 0.0160, wR_2[b] = 0.0428
R indices (all data)	R_1 = 0.0169, wR_2 = 0.0433
Extinction coefficient	n/a
Largest diff. peak and hole	0.262 and -0.211 e.Å^{-3}

[a] $R_1=\sum||F_o|-|F_c||/\sum|F_o|$, [b] $wR_2=\{\sum[w(|F_o|^2-|F_c|^2)^2]/\sum[w(F_o^2)^2]\}^{1/2}$

FTIR spectra of ligand GA and MOF Zn-GA

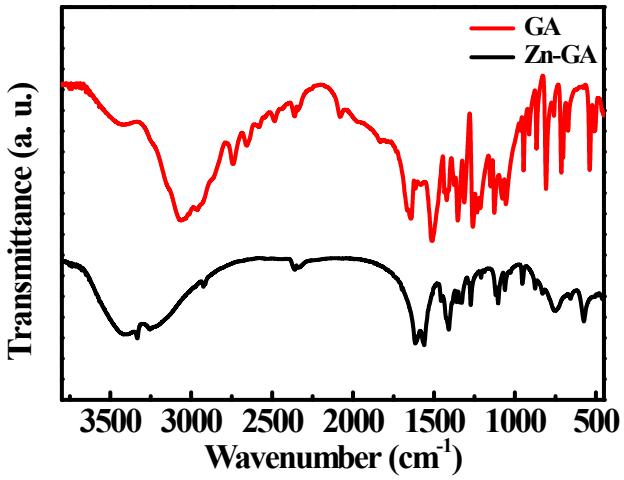

Figure S1 FTIR spectra of GA and Zn-GA

Thermogravimetric analysis of MOFs

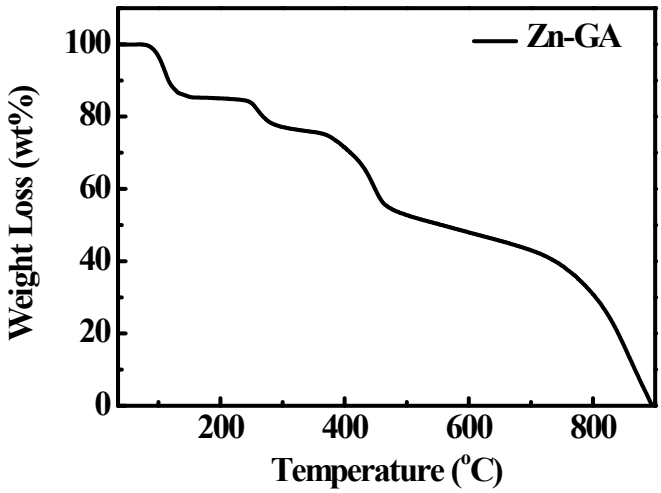

Figure S2 Thermogravimetric analysis of as-synthesized Zn-GA.

SEM images of Zn-GA

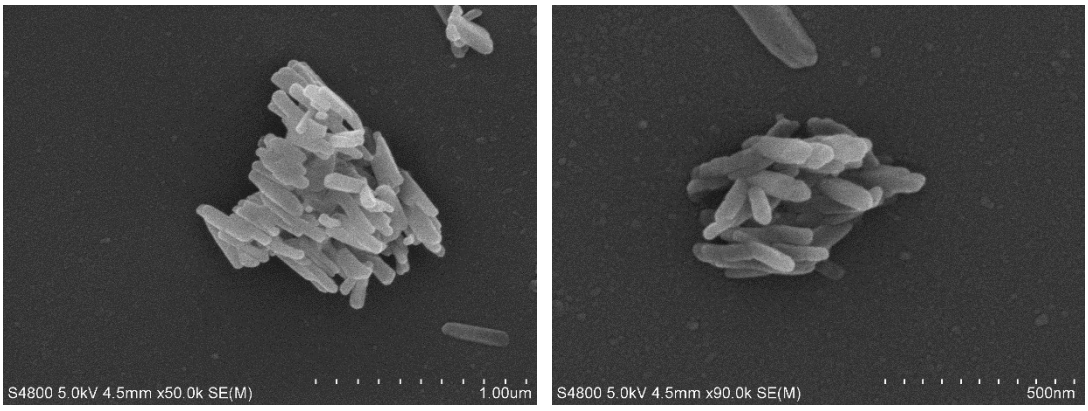

Figure S3 SEM images of as-synthesized Zn-GA

As Figure S3 shown, the SEM images revealed that the morphology of Zn-GA was bar-shaped. Meanwhile, the length of it was about 400 nm – 600 nm, and the width was about 50 nm – 200 nm.

N_2 adsorption isotherm for as-synthesized Zn-GA

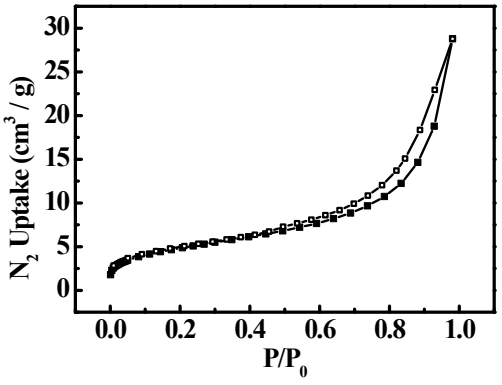

Figure S4 N_2 adsorption isotherm (77 K) for as-synthesized Zn-GA

(filled: adsorption, empty: desorption)

Drug Loading Efficiency

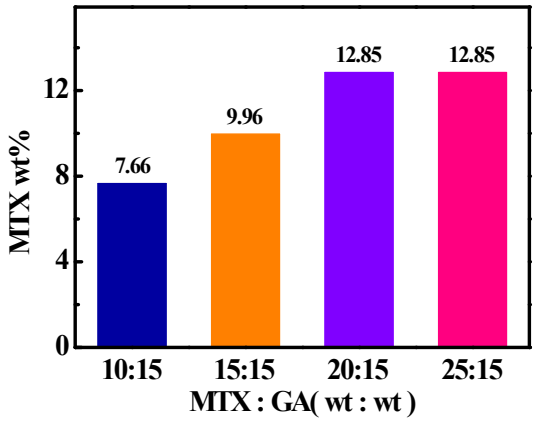

Figure S5 The payload of MTX-encapsulated Zn-GA with different ratio of MTX to GA

The anticancer drug Methotrexate (MTX) was encapsulated by one-pot synthesis, and the maximum loading reached when adding MTX (20 mg) into the reaction solution. The mixture of methotrexate, glutamic acid and $Zn(NO_3)_2 \bullet 6H_2O$ was dissolved in solution of DMF/H_2O, then the solution was heated at 80 °C for 6 days. The bright yellow MTX-loaded powders were gained.

The loading amount of MTX was estimated by ^{1}H NMR. In the ^{1}H NMR spectrum of MTX-encapsulated Zn-GA, proton signals of the alkane of ligand GA in the range 3.89-3.91 ppm (1.00 H), 2.44-2.48 ppm (0.93 H), 2.32-2.38 ppm (1.03 H) and peak 1.94-2.05 ppm (2.00 H) were observed obviously. The data also showed the proton signals from the drug MTX molecule, such as 0.08 H at 8.71 ppm ($C_4N_2C_2N_2\mathbf{H}CH_2$), 0.16 H at 7.72-7.73 ppm ($NC_6H_2\mathbf{H_2}CO$), 0.16 H at 6.84-6.86 ppm ($NC_6\mathbf{H_2}H_2CO$), 0.09 H at 4.30-4.32 ppm (N(COOH)C**H**CH_2), etc. As a result, the amount of encapsulated MTX was about 12.85 wt%.

PXRD patterns of as-synthesized Zn-GA and soaked Zn-GA

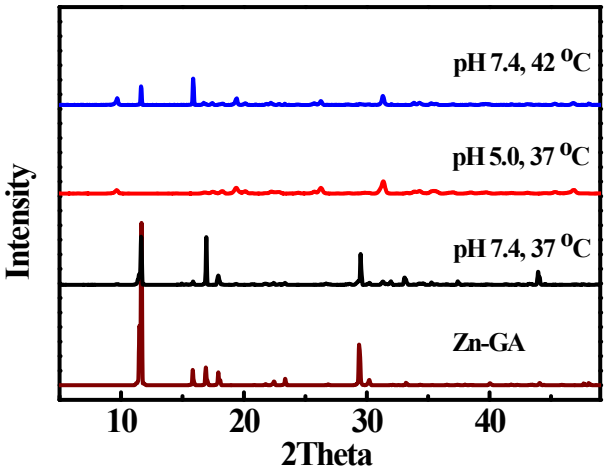

Figure S6 PXRD patterns of as-synthesized Zn-GA and Zn-GA under different physiological conditions

The toxic effect of MTX-encapsulated Zn-GA

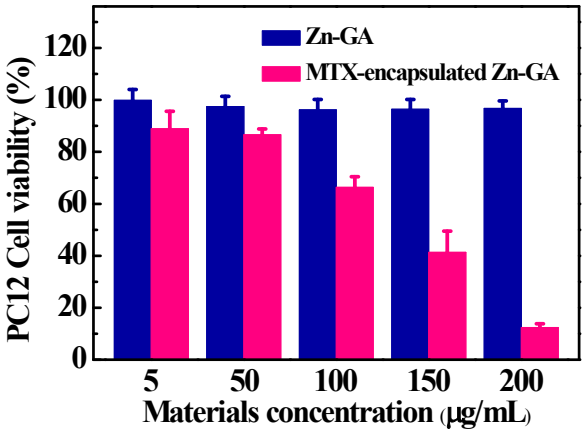

Figure S7 PC12 cell viability after exposure to Zn-GA (royal) and MTX-encapsulated Zn-GA (pink)

After drug loading, the toxicity of MTX-encapsulated Zn-GA was investigated by MTT assay against PC12 cells. The five concentrations (5, 50, 100, 150 and 200 μg/mL) were also selected

in cytotoxicity study. As Figure S7 displayed, comparing with high survival rate of PC12 cells (above 96%) which cultured with Zn-GA, MTX-encapsulated Zn-GA exhibited much lower viability and more cells were killed due to the introduction of anticancer drug MTX. About 88 % of PC12 cells were survived at the concentration of 5 μg/mL, and the survival rate reduced gradually with the increase of content. Finally, the livability of PC12 was dropped to only 12% when the material concentration was 200 μg/mL, and revealed the great toxic effects of MTX-encapsulated Zn-GA on PC12 cells.

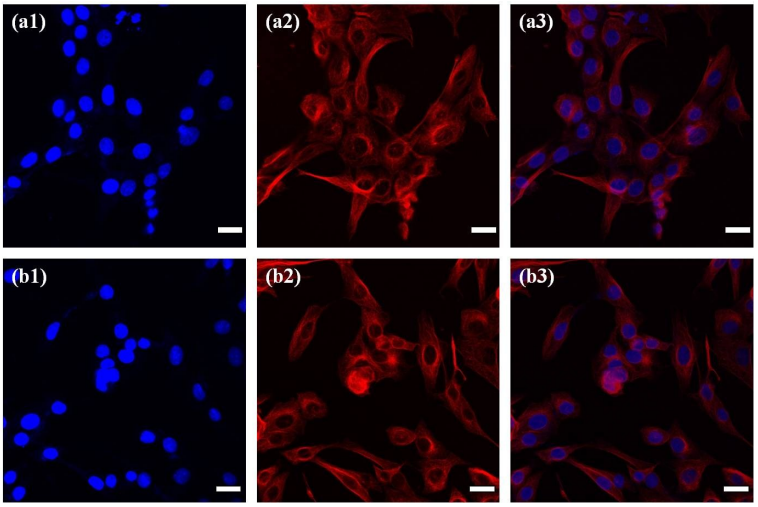

Figure S8 Confocal laser scanning microscopy images of PC12 cells incubated with MTX-encapsulated Zn-GA (a, 5 μg/mL; b, 50 μg/mL) for 24 h. (Nuclei and microtubular cytoskeleton were stained by DAPI (blue) and β-tubulin (red). Scale bar, 20 μm)

Meanwhile, the morphological informations of PC12 cells which cultured with MTX-encapsulated Zn-GA (5 μg/mL, 50 μg/mL) were investigated by confocal microscopy. As shown in Figure S8, the nucleus (blue) and microtubular cytoskeleton (red) of some fixed cells no further exhibited ideal growth states. In some cells, the nucleus seemed to be expanding and

the outstretched filamentous tubulin vanished, although a few cells remained normal states. In addition, some cells had shrunk to a small mass. Figure S8(a3) and Figure S8(b3), co-localized fluorescence graphs, exhibited the material had great toxicity after drug loading.