Electronic supplementary information for:

High-efficient elimination of intracellular bacteria via a metal organic frameworks (MOFs) based three-in-one delivery system

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Contents

1.Experimental

1.1 Synthesis of ZIF-67

In a typical synthesis of ZIF-67,[1] 0.45 g cobalt nitrate hexahydrate was dissolved in 3 mL of deionized (DI) water and 5.5 g 2-methylimidazole(2-MIM) was dissolved in 20 mL of DI water. Those two solutions were mixed and stirred for 6 h at room temperature. The resulting purple precipitates were collected by centrifuging, washed with water for 3 times, and finally vacuum-dried at 80 ℃.

1.2 Synthesis of MOF-5

In a typical synthesis of MOF-5,[2] 0.5065 g terephthalic acid (PTA) and 850 μL triethylamine were dissolved in 40 mL of DMF. 1.699 g $Zn(OAc)_2$ $2H_2O$ was dissolved in 50 mL of DMF. The zinc salt solution was added to the organic solution forming a precipitate and stirred for 3h. The precipitates were collected by centrifuging, washed with DMF for several times and finally vacuum-dried at 80 ℃.

1.3 Synthesis of HKUST-1

In a typical synthesis of HKUST-1,[3] 1.22 g $Cu(NO_3)_2$ $3H_2O$ and 0.58 g 1,3,5-benzenetricarboxylic acid (BTA) were dissolved in 5 mL dimethylsulfoxide (DMSO) to prepare precursor solution. Then 200 μL of the precursor solution was dropped into 10 mL methanol under stirring and stirring for another 10 min. The precipitate was collected by centrifugation, washed with methanol and finally vacuum-dried at 80 ℃.

1.4 Antibiotics encapsulated and HA decorated of MOFs

The one-step synthesis of Tet@ZIF-67, Tet@MOF-5 and Tet@HKUST-1, and hyaluronic acid (HA) decorated were refer to experimental section with some modification based on the above three methods.

1.5 PVP exchange[4]

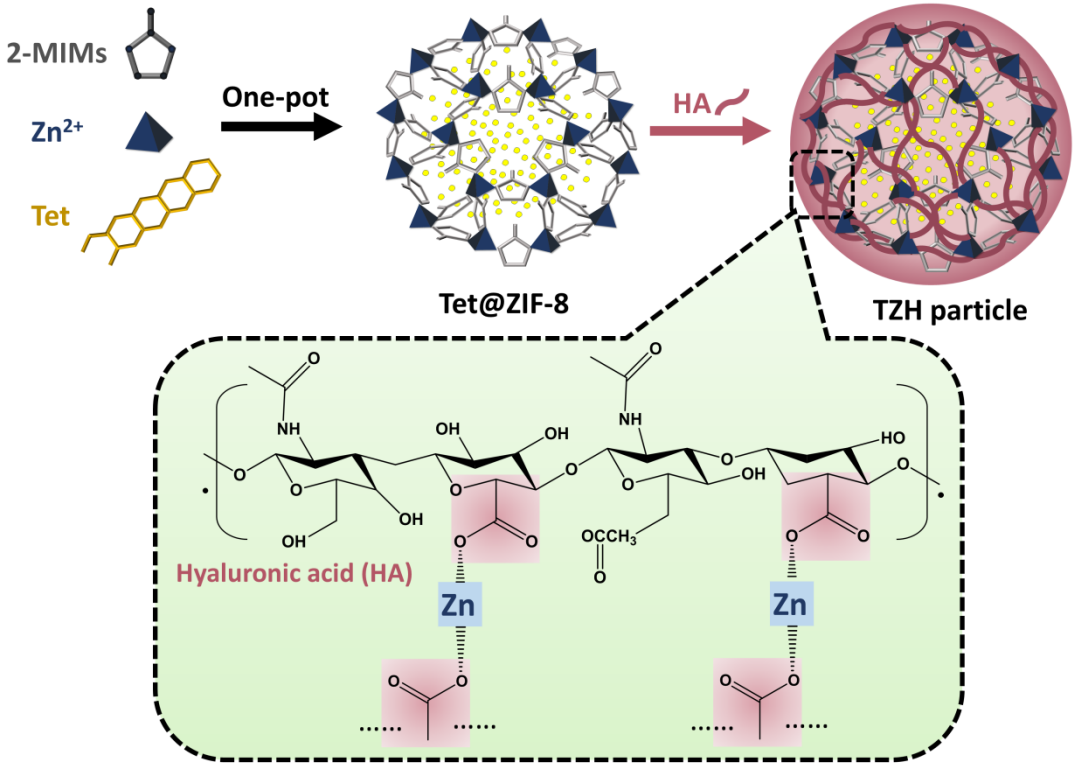
As-synthesized TZH were dispersed in 10mL of5% PVP solution, left for 10min, then centrifuged to obtain the supernatant and analyze the amount of antibiotics. This PVP exchange was repeated 2 more times.

1.6 Mediating effect of HA

To investigate the mediate function of HA in the process of cell phagocytosis, Rhodamine B (RhB) instead of Tet drugs was encapsulated in the ZIF-8 structure to prepare RhB@ZIF-8 or RhB@ZIF-8@HA. The sterile cover slips were put in 6-well culture plates and macrophages were

seeded at a density of 5 x 10^4 cells per well allowed to adhere for 12 h. The test and control materials were added to the growth media and cultured for 3 h afterwards. Then washed twice with PBS. Finally, the cells were fixed with 4% paraformaldehyde for 15 min at room temperature and washed twice with PBS again. The slides were mounted and observed with a fluorescence microscope imaging system.

2. Results and discussion



Scheme S1 Scheme of TZH synthesis.

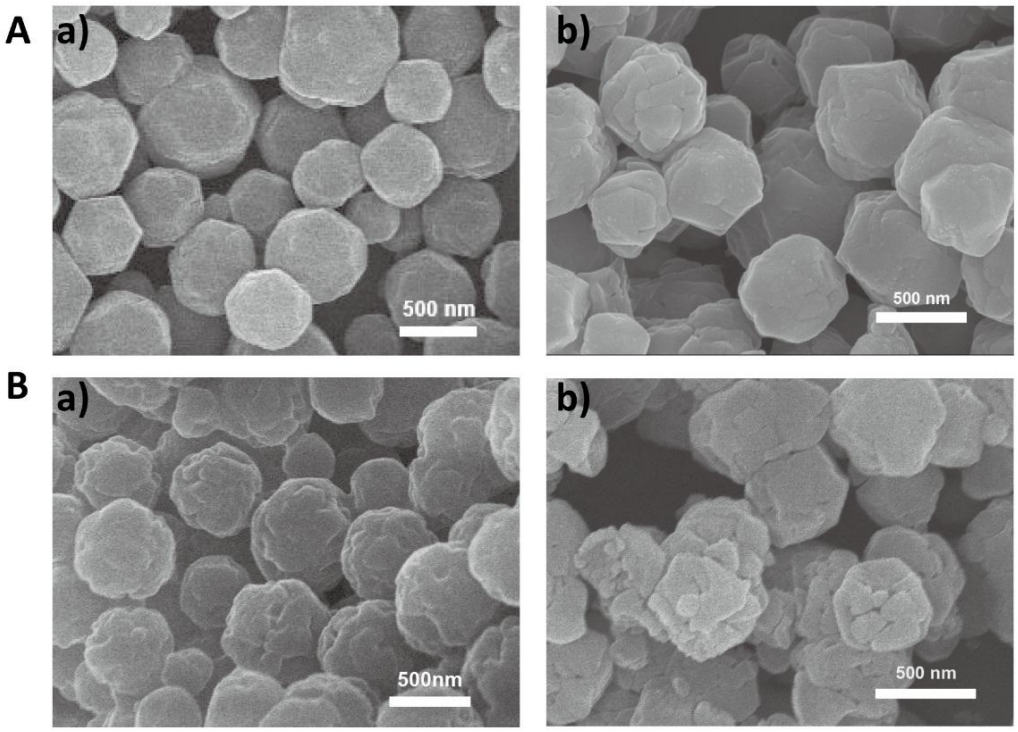


Fig. S1 SEM image of (A) ZIF-8 and (B) TZH particles. (a) and (b) are freshly prepared and left for two weeks at room temperature, respectively.

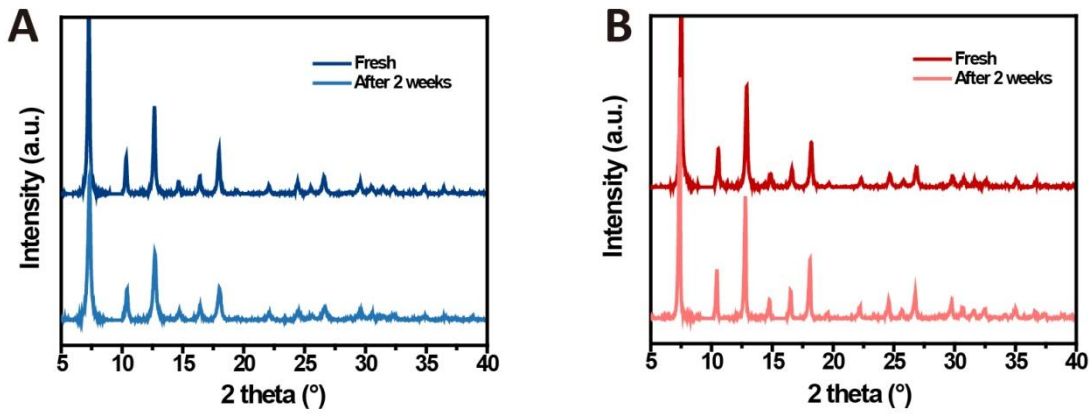


Fig. S2 XRD patterns of fresh prepared or after placed for 2 weeks at RT of(A) pure ZIF-8 and (B)TZH.

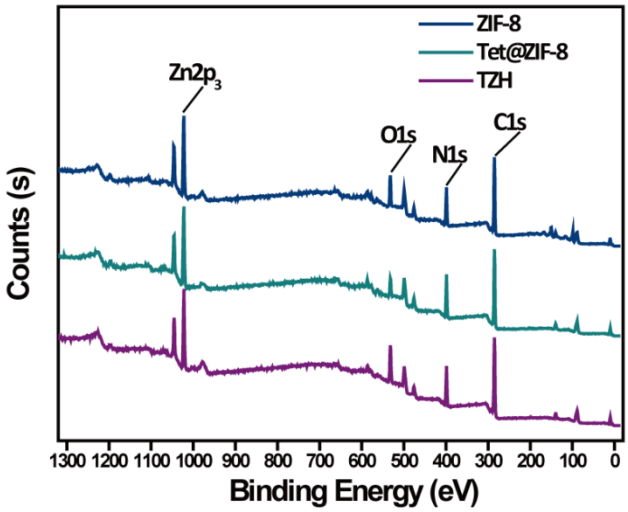


Fig. S3 XPS spectra of Zn $2p_3$, C 1s, N 1s and O 1s performed on ZIF-8,Tet@ZIF-8 and TZH.

Table S1 The binding energy regions corresponding to Zn $2p_3$, C 1s, N 1s and O 1s characteristic peaks of XPS experiments performed on ZIF-8,Tet@ZIF-8 and TZH**.**

Sample	Zn $2p_3$	C 1s	N 1s	O 1s
ZIF-8	1022.40	285.16	399.16	532.28
Tet@ZIF-8	1022.35	285.06	399.07	532.01
TZH	1022.16	285.09	399.06	531.99

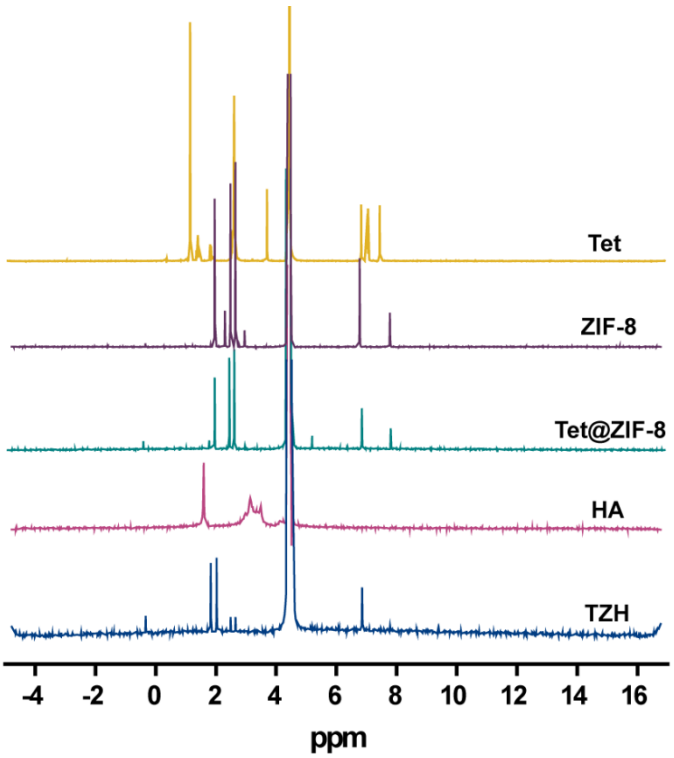


Fig. S4 ^{1}H-NMR line shape of Tet, ZIF-8, Tet@ZIF-8, HA and TZH.

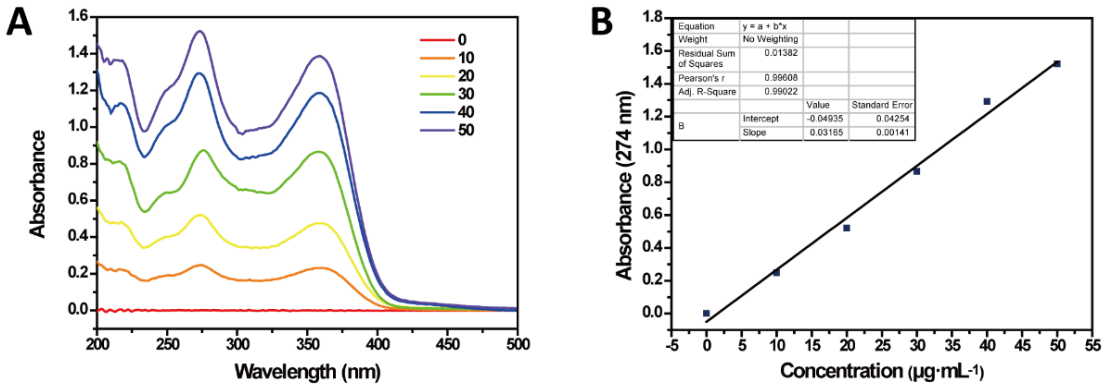


Fig.S5 The UV–vis absorption spectrum (A) and standard curve (B) of the concentration of tetracycline range from 0-50 μg·mL^{-1}.

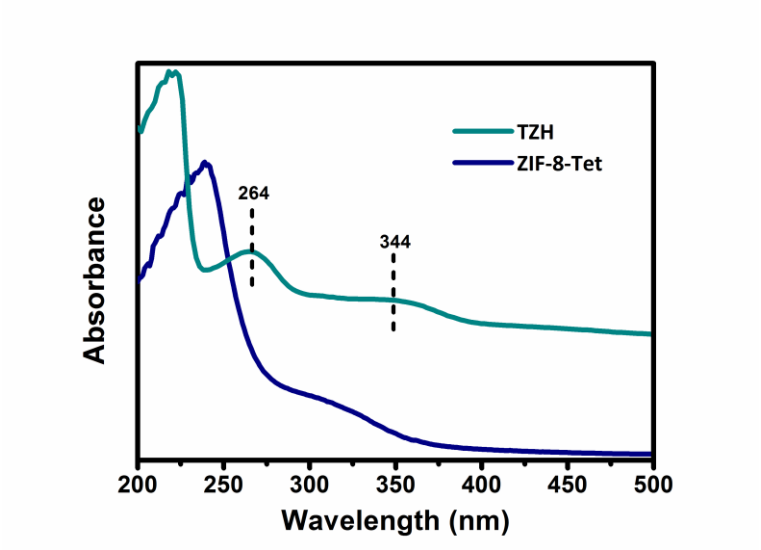


Fig. S6 UV–vis absorption spectrum of TZH(encapsulated) and ZIF-8-Tet(adsorbed).

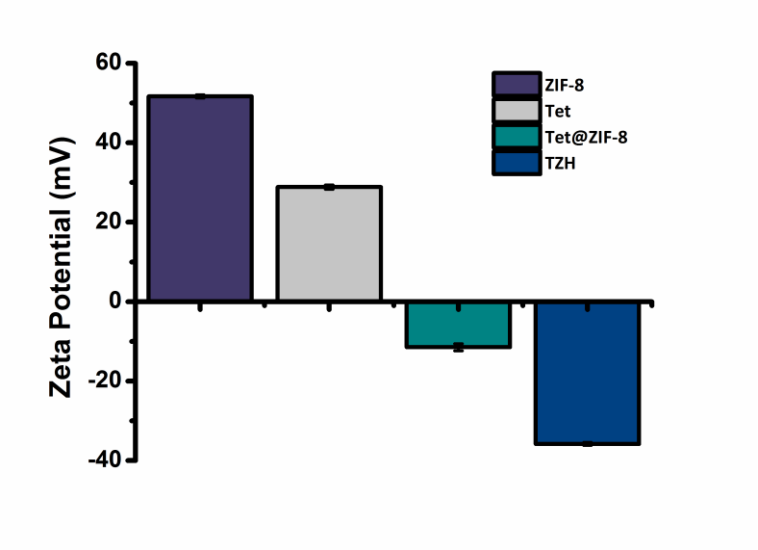


Fig. S7 Zeta potential of ZIF-8, Tet, Tet@ZIF-8 and TZH.

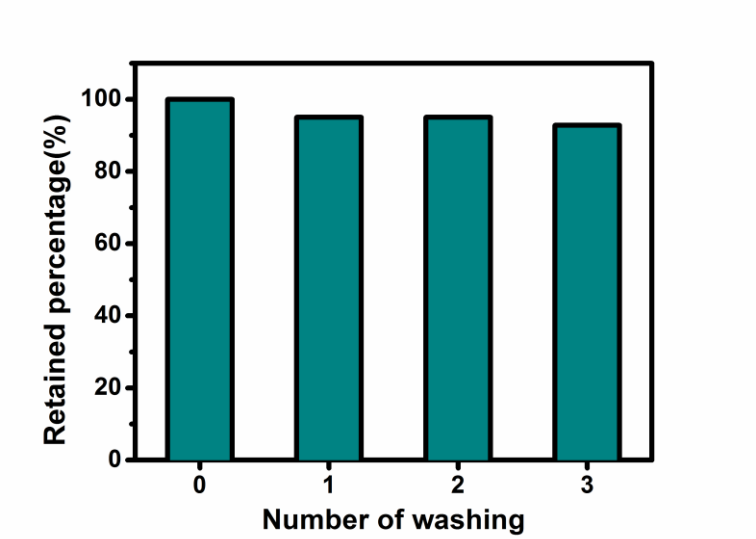


Fig. S8 PVP exchange results of TZH.

Table S2 Summary of the BET parameters of the ZIF-8, Tet@ZIF-8 and TZH

Sample	BET surface area(m^2/g)	Adsorption average pore diameter(nm)	BJH Adsorption cumulative volume of pores(cm^3/g)
ZIF-8	1,762.31	2.1552	0.131649
Tet@ZIF-8	1,779.60	2.1278	0.125499
TZH	2,034.34	2.0951	0.116224

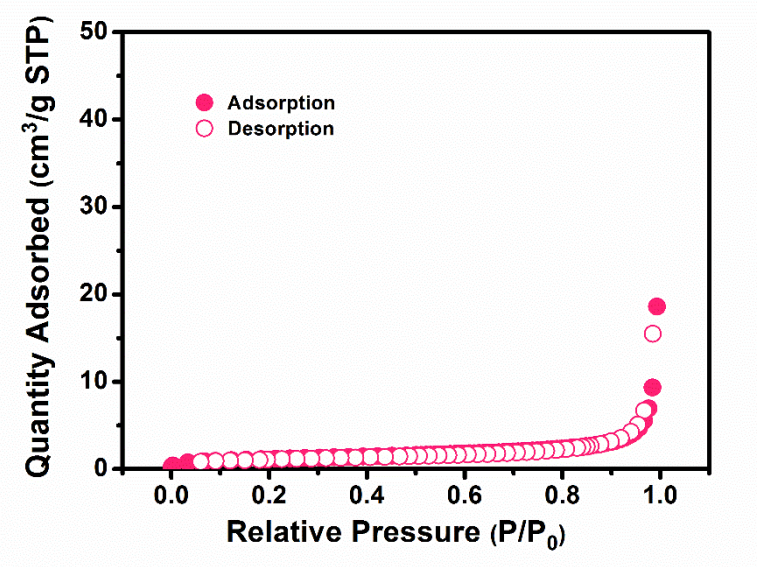


Fig. S9 N_2 adsorption/desorption isotherms of HA measured at 77 K.

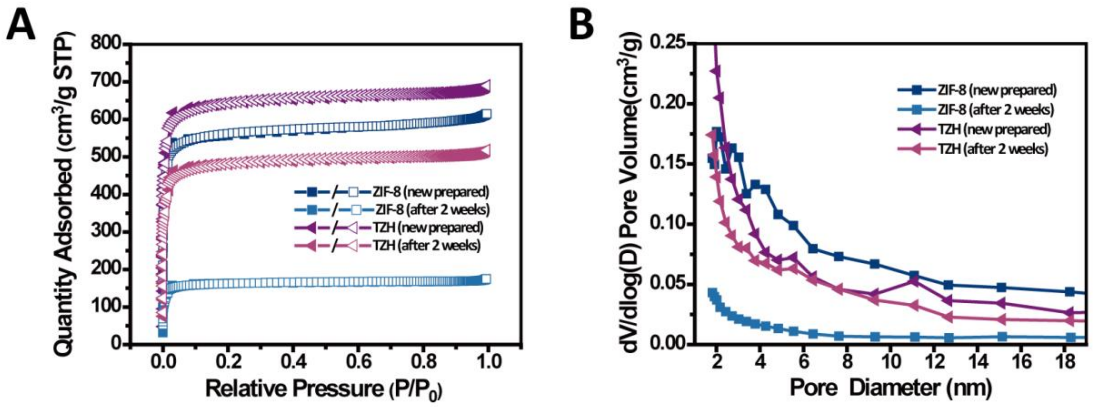


Fig. S10 (A) N_2 adsorption/desorption isotherms measured at 77 K and (B) corresponding pore size distribution calculated using BJH of ZIF-8 and TZH(new prepared or after placed for 2 weeks).

Table S3 Summary of the BET parameters ofthe ZIF-8 and TZH(new prepared or after placed for 2 weeks)

Sample		BET Surface Area (m ²/g)	Adsorption average pore diameter (nm)	BJH Adsorption cumulative volume of pores(cm^3/g)
ZIF-8	new prepared	1,762.31	2.1552	0.131649
	after 2 weeks	503.68	2.1482	0.026681
TZH	new prepared	2,034.34	2.0951	0.116224
	after 2 weeks	1,526.65	2.0958	0.083729

Table S4 The cytotoxicity of ZIF-8 or related composites to different cell types in some previous literatures

Name	Cell type	Dose/μg·mL^{-1} (cell viability)	Reference
NZIF-8	HeLa	50 (>70%)	[5]
ZIF-8	HeLa	100 (50%)	[6]
	J774	25 (50%)	
ZIF-8	MDA-MB-231 MDA-MB-468 MCF-7 NCI	250 (75−90%)	[7]
ZIF-8	HT-29 HL-60	>25 (unmeasured, 50%)	[8]
PAA@ZIF-8 NPs	MCF-7	50 (>90.8%)	[9]
ZIF-8/GO	4T1	100 (close to 100%)	[10]
TZH	RAW 264.7	50 (>80%)	This work

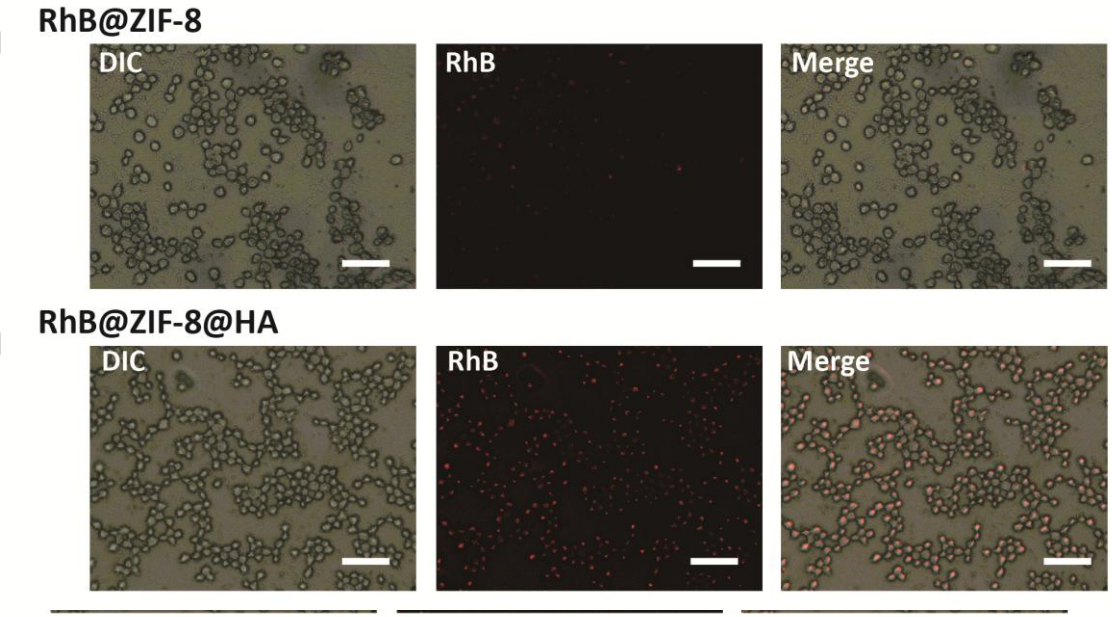


Fig. S11 Co-localization of RhB@ZIF-8@HA and macrophages. All scale bars are 50 μm.

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