Electronic Supplementary Material (ESI) for Journal of Materials Chemistry B.

Supporting Information

Controlled Release of Small Molecules and Proteins from DNA-Surfactant Stabilized Metal Organic Frameworks

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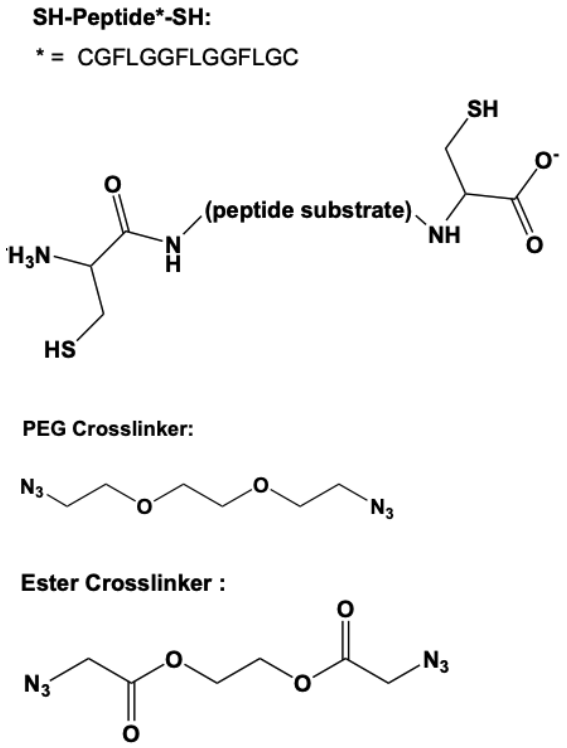

Figure S1. Peptide Crosslinkers were used to make nanoparticles for cell viability assay and confocal microscopy. Ester crosslinker is specifically used to make ZIF-8 AP SCM and ZIF-8 TAMRA SCM while the PEG crosslinker was utilized to produce nanoparticles for microscopy and toxicity studies.

Table S1. Size and surface charge analyses of different nanoparticle constructs

Nanoparticles	Size	Charge
ZIF-8	8.5 ± 1.2 nm	+24.6 ± 1.8 mV
ZIF-8 SCM (PEG)	17.4 ± 2.6 nm	+27.4 ± 2.6 mV
ZIF-8 SCM (peptide)	33.8 ± 8.2 nm	+20.4 ± 3.0 mV
ZIF-8 NAN (peptide)	48.1 ± 6.4 nm	-21.1 ± 3.5 mV
ZIF-8 TAMRA	7.2 ± 2.7 nm	+35.8 ± 6.9 mV
ZIF-8 TAMRA SCM (non-ester)	19.0 ± 5.9 nm	+28.3 ± 6.6 mV
ZIF-8 TAMRA NAN (non-ester)	31.1 ± 7.2 nm	-26.3 ± 5.1 mV
ZIF-8 TAMRA SCM (ester)	23.7 ± 8.5 nm	+12.4 ± 6.5 mV
ZIF-8 TAMRA NAN (ester)	38.1 ± 6.2 nm	-29.4 ± 3.1 mV
ZIF-8 TAMRA SCM (peptide)	61.3 ± 18.6 nm	+21.5 ± 3.8 mV
ZIF-8 TAMRA NAN (peptide)	76.3 ± 7.3 nm	-29.6 ± 3.7 mV
ZIF-8 FI	7.9 ± 1.9 nm	+39.6 ± 2.8 mV
ZIF-8 FI SCM (non-ester)	29.3 ± 2.3 nm	+45.8 ± 4.3 mV
ZIF-8 Fluorescein NAN (non-ester)	41.4 ± 2.3 nm	-35.2 ± 4.6 mV
ZIF-8 CPT	8.3 ± 2.7 nm	+72.5 ± 12.0 mV
ZIF-8 CPT SCM (peptide)	44.4 ± 11.5 nm	+14.1 ± 3.3 mV
ZIF-8 CPT NAN (peptide)	29.5 ± 6.1 nm	-24.4 ± 3.7 mV
ZIF-8 CPT SCM (non-ester)	34.0 ± 10.5 nm	+31.2 ± 5.8 mV
ZIF-8 CPT NAN (non-ester)	43.3 ± 12.4 nm	-43.4 ± 8.6 mV
ZIF-8 AP	175.9 ± 34.1 nm	+7.6 ± 5.6 mV
ZIF-8 AP SCM (ester)	71.1 ± 22.7 nm	+27.5 ± 3.1 mV

ZIF-8 EGFP	85.0 ± 12.8 nm	+30.9 ± 6.2 mV
ZIF-8 EGFP SCM (ester)	24.4 ± 18.0 nm	+32.2 ± 4.1 mV
ZIF-8 EGFP NAN (ester)	40.0 ± 19.4 nm	-40.8 ± 4.7 mV
ZIF-8 EGFP SCM (non-ester)	31.5 ± 9.3 nm	+28.2 ± 5.2 mV
ZIF-8 EGFP NAN (non-ester)	42.3 ± 12.0 nm	-37.7 ± 3.1 mV
ZIF-8 EGFP SCM (peptide)	68.4 ± 19.0 nm	+17.6 ± 4.7 mV
ZIF-8 EGFP NAN (peptide)	74.3 ± 14.0 nm	-29.3 ± 4.9 mV

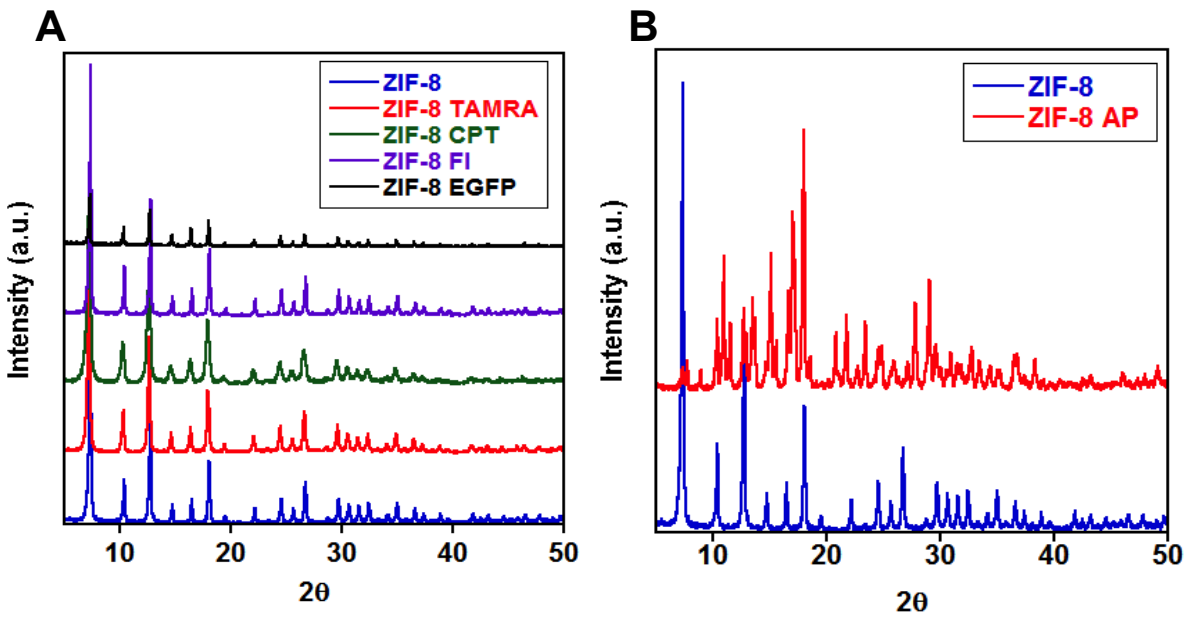

Figure S2. (A) PXRD spectra of ZIF-8 with different cargo shown retaining the characteristic peak pattern for an empty ZIF-8 MOF. The ZIF-8 PXRD spectrum is consistent with those reported in simulations and literatures.[2-4] (**B)** PXRD spectrum comparison between ZIF-8 and ZIF-8 AP.

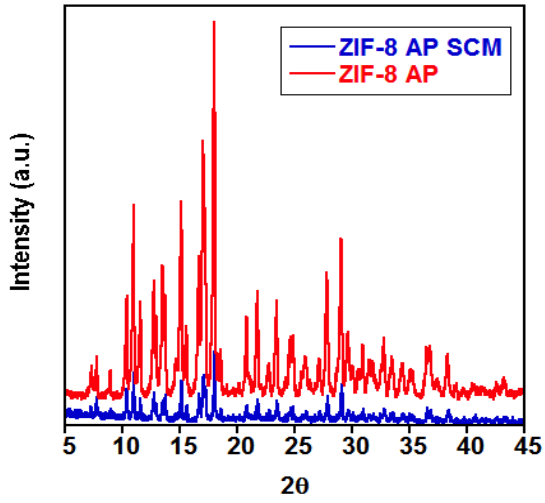

Figure S3. PXRD spectrum comparison between ZIF-8 AP and ZIF-8 AP SCM showing the preservation of ZIF-8 AP crystallinity and the influence of the protein cargo on the overall structure.

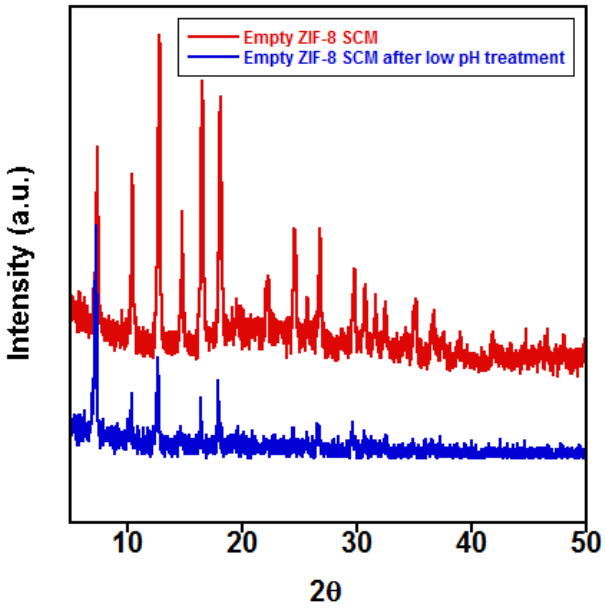

Figure S4A. PXRD spectrum indicating the retention of ZIF-8 crystal structure inside the SCM even after incubating at low pH (0.10 M pH 5.20 sodium acetate buffer) for an hour.

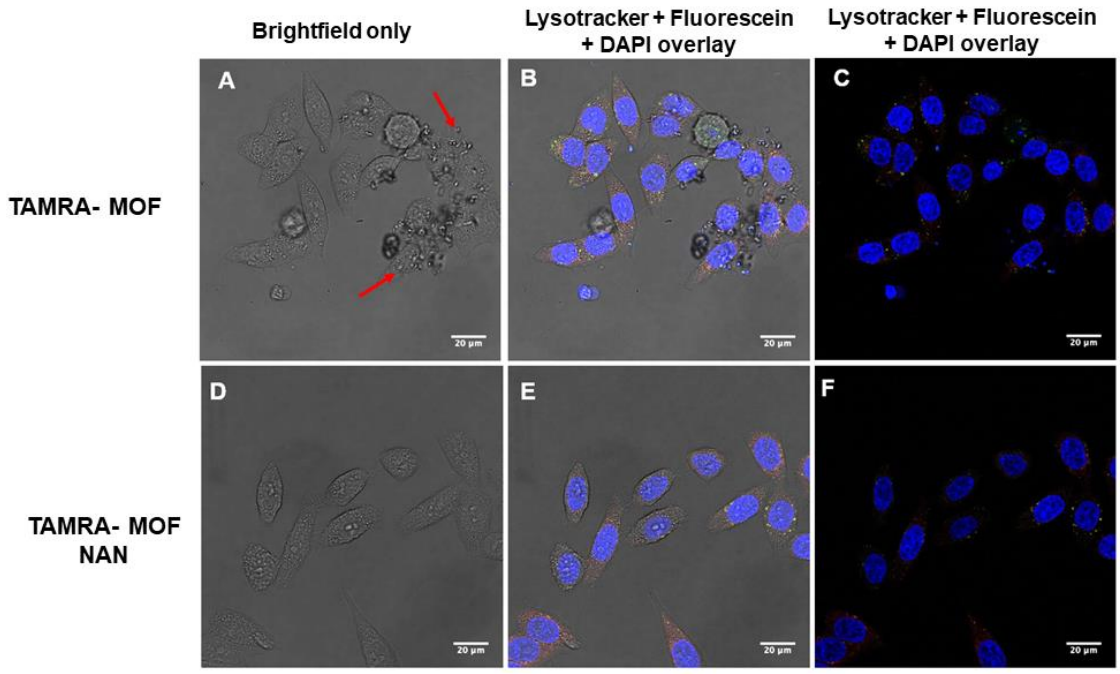

Figure S4B. Confocal study of TAMRA MOFs and TAMRA MOF-NANs in 10% FBS serum post 30 min incubation. A-C Representative brightfield and confocal imaging of TAMRA loaded MOFs as seen under **A**) brightfield imaging in which debris is noted in confocal images by red arrows **B**) multichannel overlay **C**) multichannel overlay darkfield. D-F representative brightfield and confocal imaging of TAMRA loaded MOF-NANs where **D**) brightfield only where no debris was observed **E**) multichannel overlay **C**) multichannel overlay darkfield.

Table S2. **Cargo content of different ZIF-8**

Cargo	Mass Yield (mg)	µg cargo / mg sample	Percent weight	Loading efficiency (%)
TAMRA	14.68	36.90	3.690	27.08
CPT	17.85	25.84	2.584	23.06
AP	13.63	163.8	16.38	89.30
EGFP Plasmid	1.134	22.01	2.201	99.85

The µg of cargo per mg of sample was determined from the concentrations of cargo calculated using standard calibration curves (see **Figure S6** below) and weights of samples.

$$\frac{\textbf{µg cargo}}{\boldsymbol{mg\ sample}} = \frac{\mu g\ cargo}{weight\ sample\ (mg)}$$

$$\boldsymbol{Percent\ weight} = \frac{mg\ cargo}{mg\ sample}\ x\ 100$$

Loading efficiencies for ZIF-8 TAMRA, CPT and AP were obtained by comparing the amount of cargo in ZIF-8 to the initial amount.

$$\boldsymbol{Loading\ efficiency}\ (\%) = \left(\frac{\frac{mg\ cargo}{mg\ sample}\ x\ total\ mg\ sample}{initial\ mg\ cargo}\right) X100$$

The loading efficiency for eGFP plasmid was obtained by determining the concentration of unencapsulated plasmid in the washings and subtracting it from initial plasmid concentration.

$$\boldsymbol{Loading\ Efficiency}\ (\%)\ \boldsymbol{for\ EGFP\ Plasmid}$$

$$= \frac{(Initial\ plasmid\ concentration - Plasmid\ Concentration\ in\ washings)}{Initial\ Plasmid\ Concentration}\ x\ 100$$

The amount of plasmid in the MOF NAN construct is calculated based from the amount of plasmid MOF incorporated in the NAN (~35 μg / mL plasmid MOF in 10 μM NAN) and the amount of plasmid encapsulated in the MOF (22.01 μg plasmid / mg plasmid MOF). See calculation below:

$$35\ \frac{\mu g\ plasmid\ MOF}{mL}\ x\ \frac{1\ mg}{1000\ \mu g}\ x\ \frac{22.01 \mu g\ plasmid}{1\ mg\ plasmid\ MOF} =$$ 0.77μg plasmid

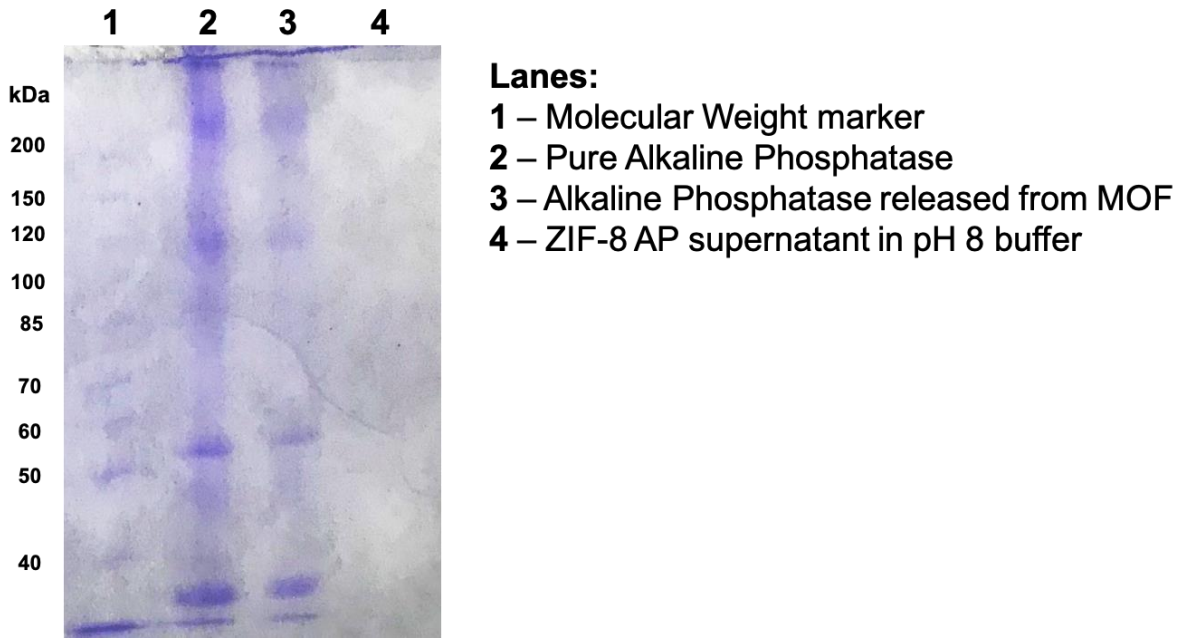

Figure S5. SDS-PAGE (7.5%) profile confirming the presence of alkaline phosphatase (AP) in the ZIF-8 MOF. Five mg of ZIF-8 AP was treated with 0.10 M pH 5.2 sodium acetate buffer for an hour to allow the degradation and release of AP. The AP was concentrated using centrifuge filters (30 kDa cutoff). **Lane 1** Molecular weight marker **Lane 2** pure AP. **Lane 3** AP liberated from ZIF-8. **Lane 4** Supernatant from ZIF-8 AP treated with non-degrading condition (40 mM pH 8.0 Tris-HCl buffer) for an hour. The gel was run for 35 minutes at 300 V, followed by with Coomasie Blue staining. The gel profile is consistent with what has been reported in literature. [5]

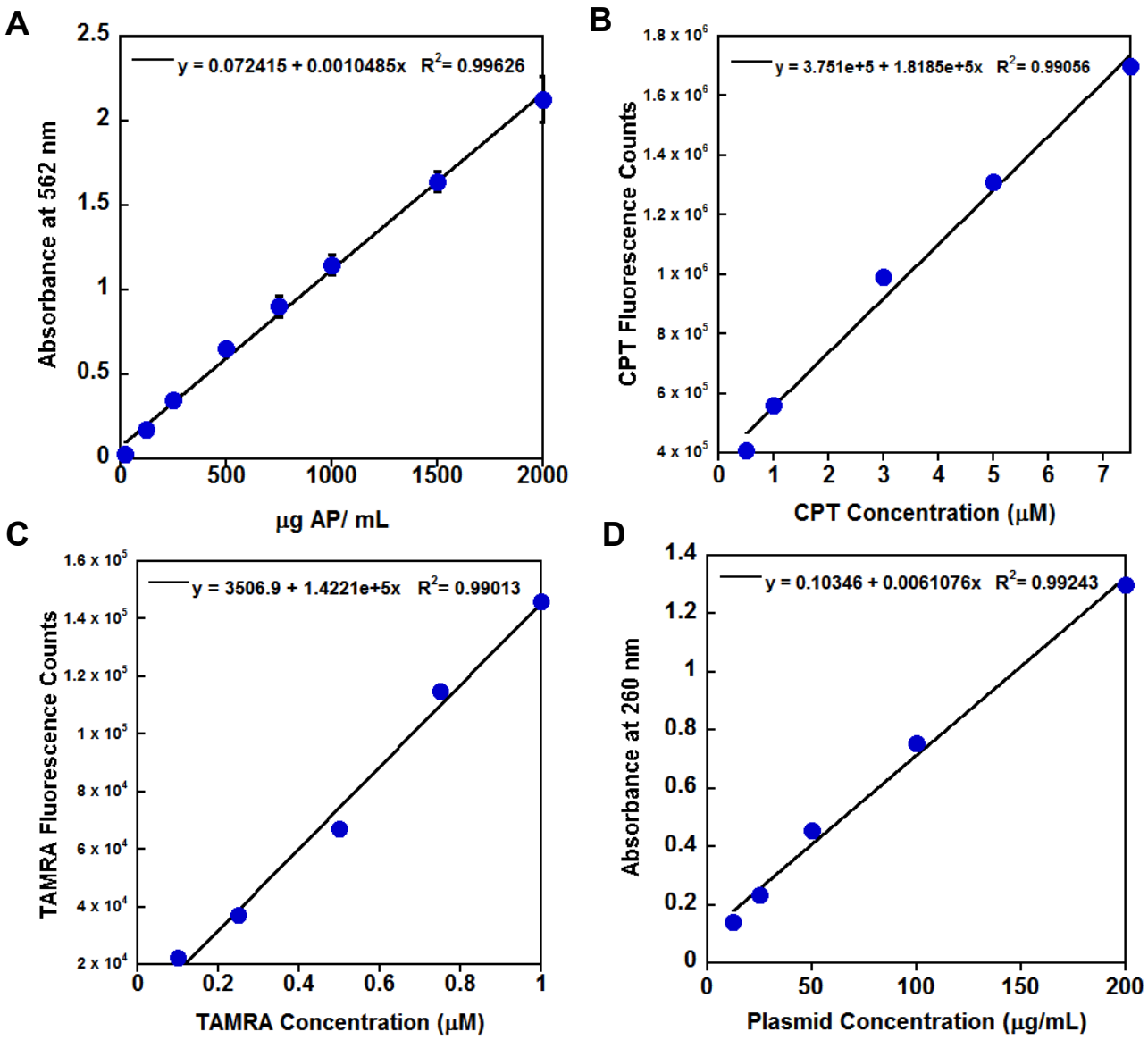

Figure S6. Calibration curves for different ZIF-8 cargo. **(A)** AP **(B)** CPT **(C)** 5-TAMRA **(D)** eGFP Plasmid

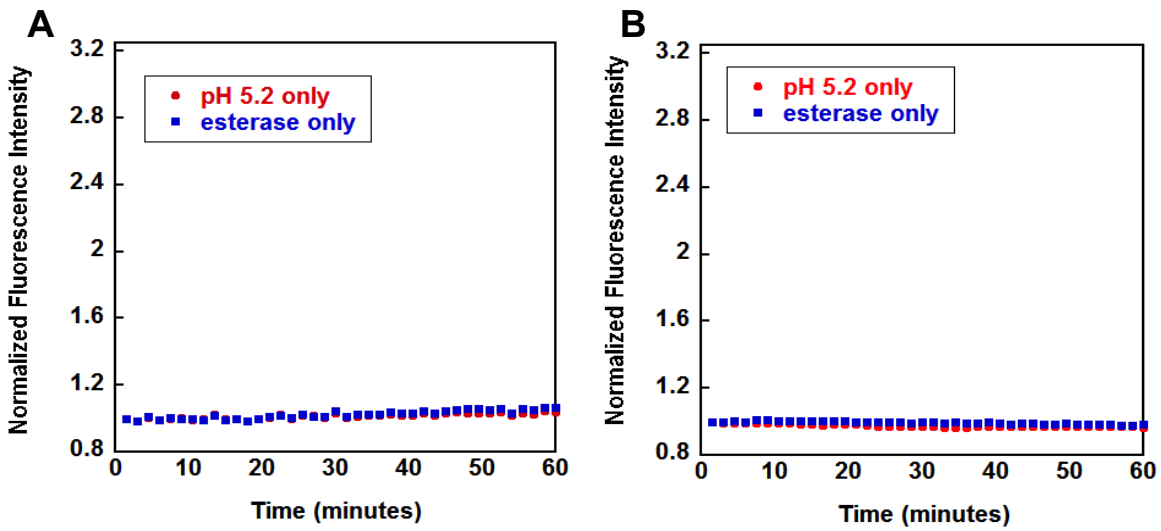

Figure S7. 5-*TAMRA Release Kinetics Assay* (A) Treatment of ZIF-8 TAMRA SCM (ester) with either pH 5.2 or esterase only showing no release of 5-TAMRA indicating the need for dual stimuli. **(B)** Similarly, no 5-TAMRA release was observed after incubating the ZIF-8 TAMRA SCM (PEG-crosslinked) with either pH 5.2 or esterase only.

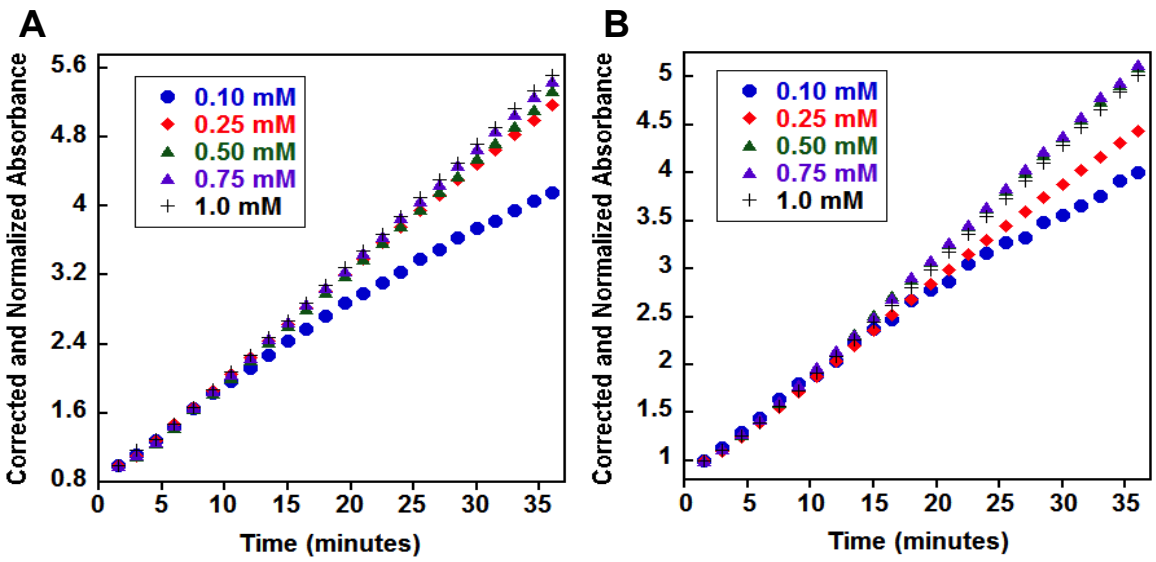

Figure S8. Enzyme (AP) Kinetics Assay (A) Trial 2 **(B)** Trial 3 of PNPP hydrolysis assay of AP released from ZIF-8 SCM after treatment with pH 5.2 and 4 units of esterase. Trial 1 shown in **Figure 5D** of the main text.

Michaelis-Menten model (see equation below) was utilized in determining the kinetic parameters of PNPP hydrolysis by post released AP.

$$V = \frac{Vmax\ [S]}{Km + [S]}$$

where V = rate, Vmax = maximum rate, [S] = substrate concentration, Km = [S] at ½ Vmax

The Michaelis-Menten fit was performed on the experimental kinetics data using Kaleidagraph software. Kinetic parameters were then calculated from the obtained equation, R = 0.99692 (see equation below).

$$V = \frac{0.1445\ [S]}{0.06475 + [S]}$$

Table S3. Kinetic parameters of PNPP hydrolysis by released AP

Kinetic Parameter	
V_{max}	0.1445 min^{-1}
K_M	0.06475 mM
k_{cat}	963.3 min^{-1} mM^{-1}
Catalytic efficiency	14878 min^{-1}

*$[AP]_{total}$ = 0.150 µM

The turnover number, k_{cat} and catalytic efficiency were calculated using the equations below.

$$kcat = \frac{Vmax}{[AP]total}$$

$$catalytic\ efficiency = \frac{kcat}{Km}$$

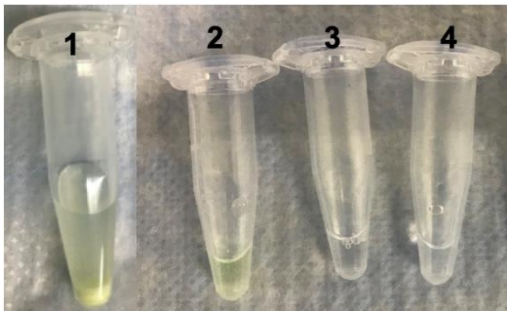

Figure S9 (1) ZIF-8 AP + substrate (2) ZIF-8 AP SCM + esterase + substrate (3) ZIF-8 AP SCM + substrate (4) esterase + substrate. Unmasking the ZIF-8 AP SCM with esterase allows the clear substrate (PNPP) to diffuse into the ZIF-8 MOF and be converted to the bright yellow product (PNP). All nanoparticles are dispersed in 40 mM pH 8.0 Tris-HCl buffer with 1 mM $MgCl_2$.

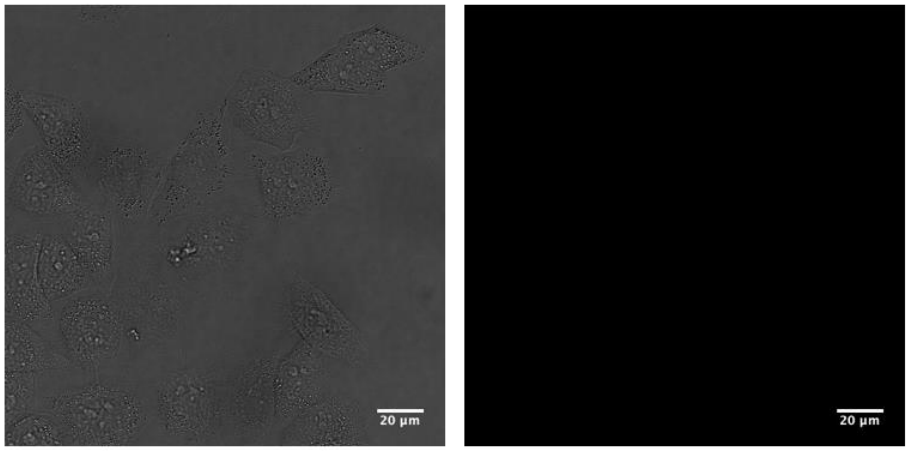

Figure S10 Confocal bright field image of HeLa cells incubated with eGFP-plasmid loaded MOF-NANs crosslinked with the non-degradable PEG crosslinker (left), darkfield image 16ft he same cells using darkfield (right). Both images viewed using the green fluorescence channel (488 nm laser) for imaging eGFP expression.

References

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