

Supplementary Information

Dual endogenous stimuli-response promoting enhanced circulate enzyme catalytic-chemotherapy via Fe₃O₄@enzymes@ZIF-8 nanocomposites

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Experimental details

Synthesis of GOx@ZIF-8: 4 mg PVP, 2 mL 160mM 2-methylimidazole and 2 mL 40 mM zinc nitrate have been added to a 1 mL 1 mg/mL GOx aqueous solution for stirring 5 min. Then, the products have been purified at room temperature for 8 hours and centrifugated at 6000 rpm for 10 min to obtain the final products.

Folic acid functionalization of GOx@ZIF-8 nanocomposites: 8.0 mg folic acid, 6.4 mg EDC and 3.8 mg NHS have been added to 10 mL PBS solution for stirring 8 h at room temperature to obtain FA-NHS. 1 mL 20 mg/mL BSA solution was mixed the FA-NHS solution. After reacting 4 h, the BSA-FA solution was purified via centrifugal ultrafiltration and finally dissolved in the MilliQ water. 10 μL BSA-FA solution has been incubated with 1 mL GOx@ZIF-8 for 6h and centrifugated three times at 6000 rpm for 10 min to obtain the product.

Enzyme catalytic therapy of HeLa cell: Enzyme catalytic therapy of HeLa cell via GOx@ZIF-8 can be evaluated by MTT approach. Firstly, 10% fetal bovine serum DMEM culture medium was adopted for preparing GOx@ZIF-8 suspension. In the 96-well plate, the zeroing group, the control group, and the experimental group were set up. 5 parallel wells were set up in each group. 100 μL of DMEM medium and HeLa cell suspension were added to each well in the zeroing group and each well in the other groups, respectively. After 24 hours, 10 μL MilliQ water was added to each well in the control group. 10 μL

GOx@ZIF-8 suspension were added to each well in the experimental group, respectively. After 24 hours, 10 μ L of MTT solution (5 mg/mL) was added to each well. After 4 h, 100 μ L of formazan solution has been added to each well for 4 h, and absorbance at 562 nm was measured by a HEALES microplate reader (MB-580).

Enzyme catalytic therapy and chemotherapy of HeLa cell: Enzyme catalytic therapy combined with chemotherapy of HeLa cell via GOx@ZIF-8 with DOX with different concentration can be evaluated by MTT approach. Firstly, 10% fetal bovine serum DMEM culture medium was adopted for preparing GOx@ZIF-8 suspension with DOX (0, 5 mg/L, 15 mg/L, 25 mg/L, 50 mg/L, 75 mg/L). In the 96-well plate, the zeroing group, the control group, and the experimental group were set up. 5 parallel wells were set up in each group. 100 μ L of DMEM medium and HeLa cell suspension were added to each well in the zeroing group and each well in the other groups, respectively. After 24 hours, 10 μ L MilliQ water was added to each well in the control group. 10 μ L GOx@ZIF-8 suspension with DOX (0, 5 mg/L, 15 mg/L, 25 mg/L, 50 mg/L, 75 mg/L), were added to each well in the experimental group, respectively. After 24 hours, 10 μ L of MTT solution (5 mg/mL) was added to each well. After 4 h, 100 μ L of formazan solution has been added to each well for 4 h, and absorbance at 562 nm was measured by a HEALES microplate reader (MB-580).

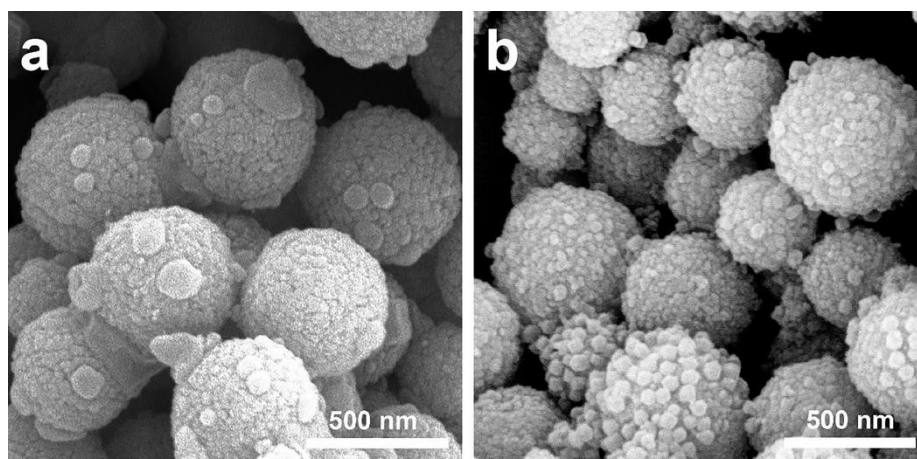


Fig. S1 a: SEM images of a: $\text{Fe}_3\text{O}_4@\text{ENZ}@\text{ZIF-8}$; b: $\text{Fe}_3\text{O}_4@\text{BiENZ}@\text{ZIF-8}$ nanocomposites.

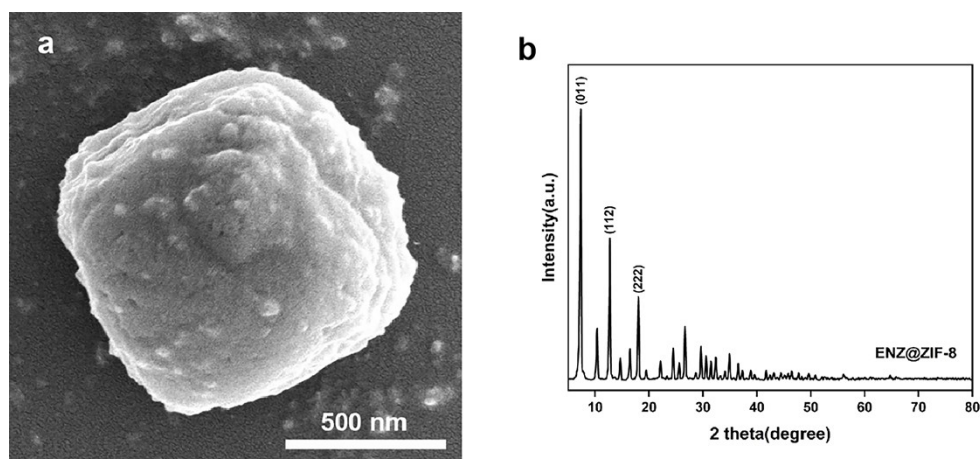


Fig. S2 a: SEM image of $\text{ENZ}@\text{ZIF-8}$ nanocomposites; b: XRD spectra of $\text{ENZ}@\text{ZIF-8}$ nanocomposites, ENZ specifically means GOx enzyme

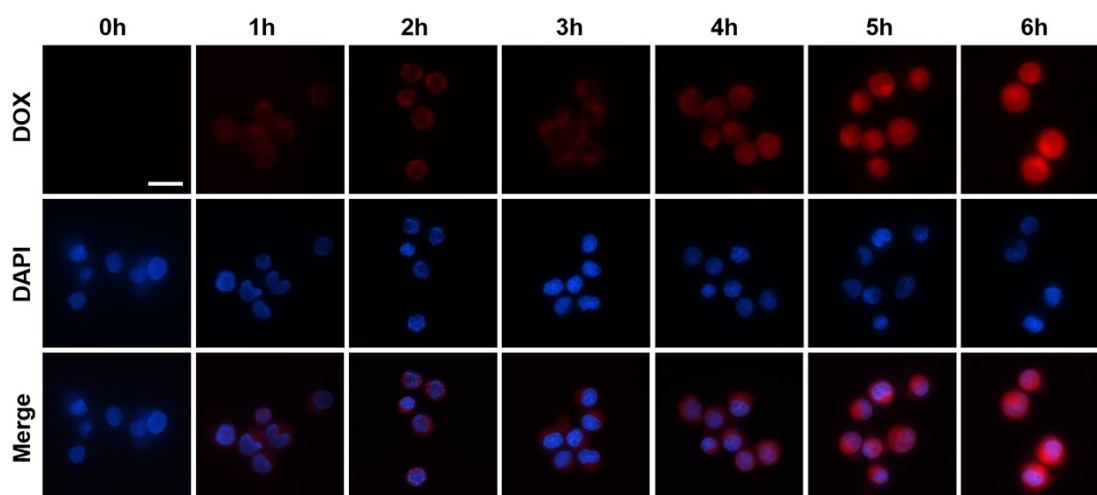


Fig. S3 Fluorescence image of ENZ@ZIF-8 nanocomposites in HeLa cell. Scale bar is 20 μm , ENZ specifically means GOx enzyme

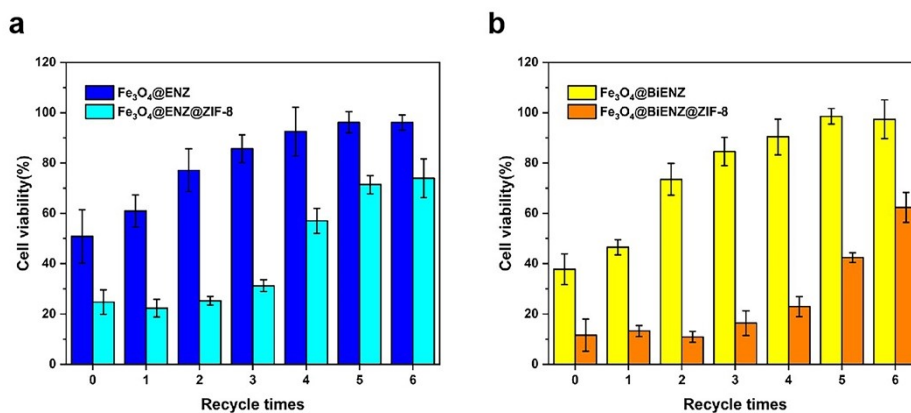


Fig. S4 a: Cell viability of $\text{Fe}_3\text{O}_4\text{@ENZ}$, $\text{Fe}_3\text{O}_4\text{@ENZ@ZIF-8}$ loading 5mg/L DOX via enzymatic-chemotherapy at different cycle from 0 to 6 times; b: $\text{Fe}_3\text{O}_4\text{@BiENZ}$, $\text{Fe}_3\text{O}_4\text{@BiENZ@ZIF-8}$ nanocomposites by enzymatic-chemotherapy at different cycle from 0 to 6 times.

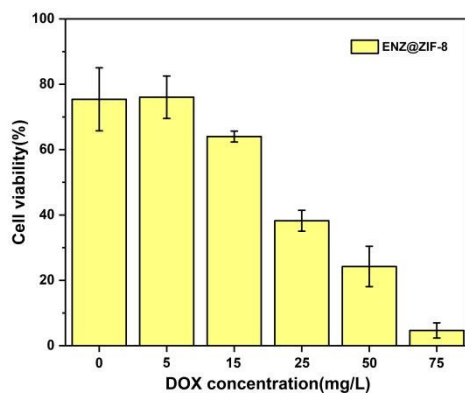


Fig. S5 Cell viability of ENZ@ZIF-8 nanocomposites by chemotherapy combined with enzymatic therapy. ENZ specifically means GOx enzyme