Supporting Information

mTORC1-dependent TFEB nucleus translocation and pro-survival autophagy induced by zeolitic imidazolate framework-8

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Notes

The authors declare no competing financial interest.

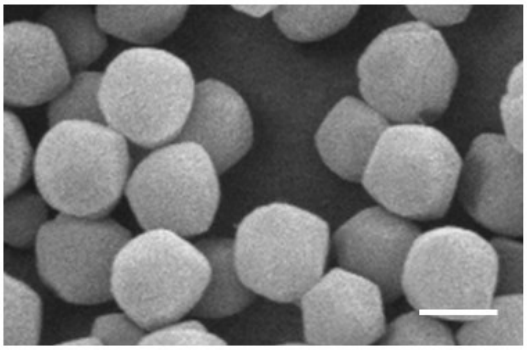

Figure S1. Scanning electron microscope (SEM) images of ZIF-8. Scale bar: 100 nm.

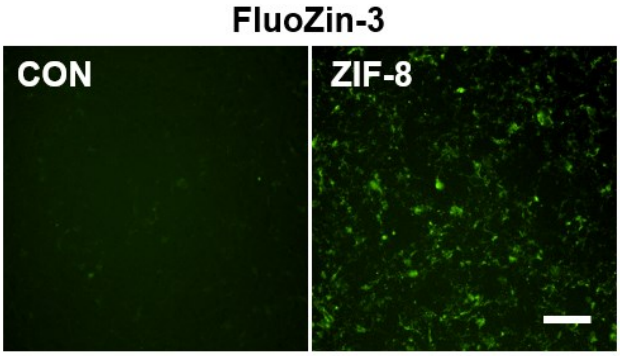

Figure S2. Representative images of Zn^{++} in HeLa cells stained by FluoZin-3 probe with treatments of PBS (CON) or ZIF-8 for 4h. Scale bar: 100 nm.

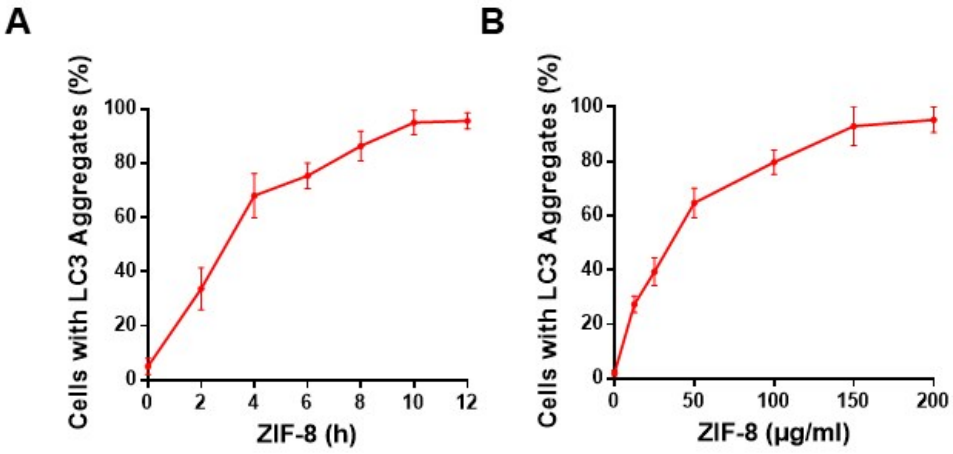

Figure S3. Statistical analysis of rates of GFP-LC3 dot aggregations after treatments in HeLa GFP-LC3 cells with 100 μg mL^{-1} ZIF-8 in time course (A) or at various concentrations of ZIF-8 for 6 h (B).

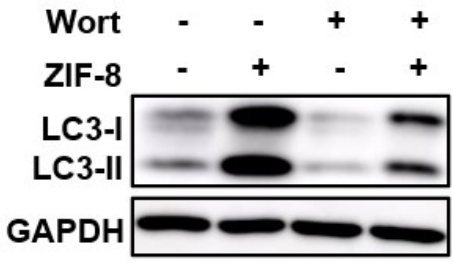

Figure S4. Western blotting analysis of LC3 after treatments with PBS or 100 μg mL $^{-1}$ ZIF-8 in HeLa cells for 10h with or without 1 mM wortmannin (Wort).

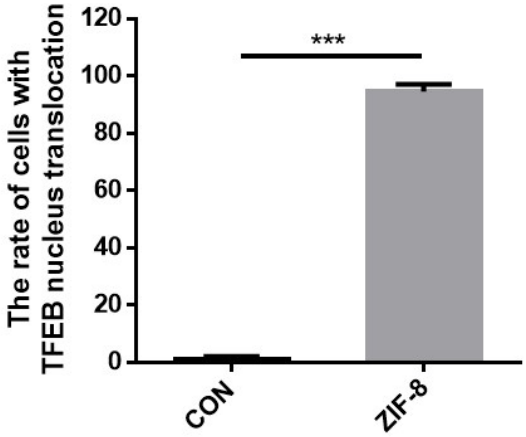

Figure S5. Statistical results of the rate of cells with TFEB nucleus translocation after PBS (CON) or ZIF-8 treatments for 6 h in HeLa TFEB cells, by counting at least 300 cells from fluorescent images.

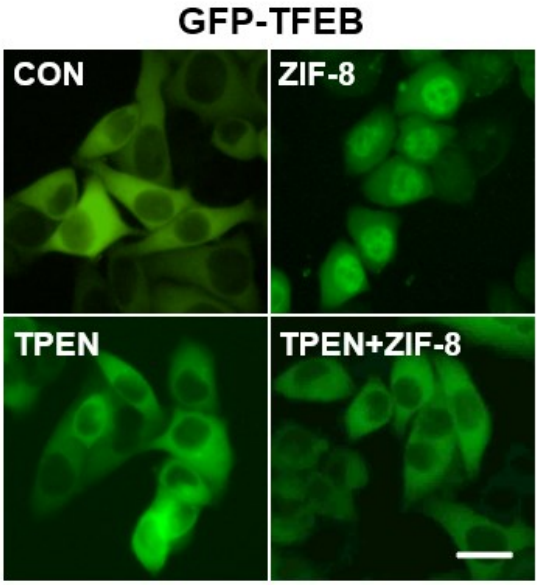

Figure S6. Representative fluorescence images after treating HeLa GFP-TFEB cells with PBS (CON) or 100 μg mL $^{-1}$ ZIF-8 for 6 h in the presence or absence of TPEN. Scale bar: 20 μm.

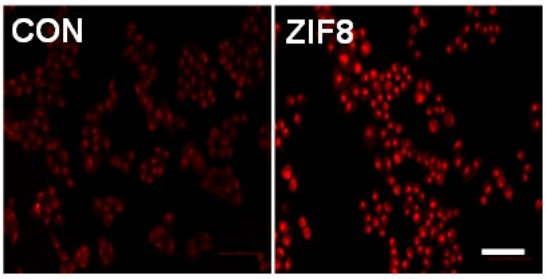

Figure S7. Representative fluorescent images after treating HeLa cells with PBS (CON) or 100 μg mL $^{-1}$ ZIF-8 for 10 h before dying lysosomes with 5 μM LysoTracker Red for 30 min. Scale bar: 100 μm.

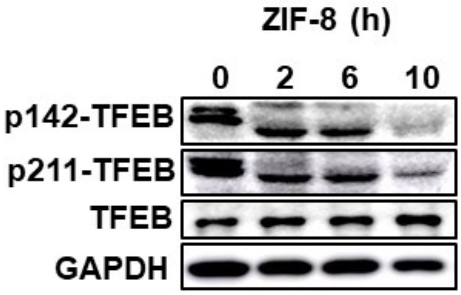

Figure S8. Western blotting test of phosphor-TFEB (Ser142), phosphor-TFEB (Ser211) and total TFEB in HeLa cells after treatments with 100 μg mL $^{-1}$ ZIF-8 for different time.

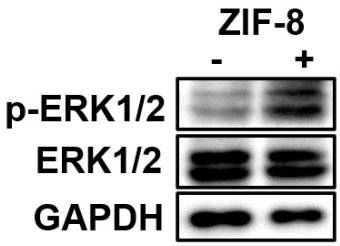

Figure S9. Western blotting analysis of phosphor -ERK 1/2 and total ERK 1/2 with or without ZIF-8 treatment at 100 μg mL $^{-1}$ for 4 h in HeLa cells.

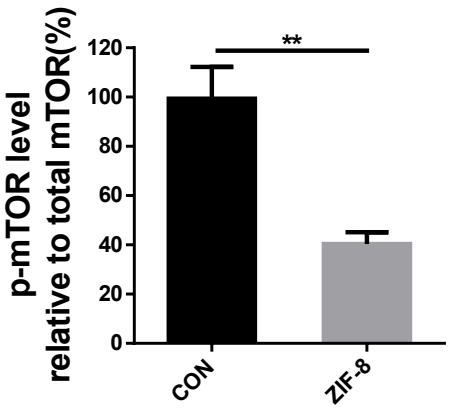

Figure S10. The level of phosphorylated mTOR (serine-2448) proteins relative to total mTOR proteins was quantified by statistical analysis basing on western blotting results with or without 100 μg mL $^{-1}$ ZIF-8 treatment for 4 h in HeLa cells.

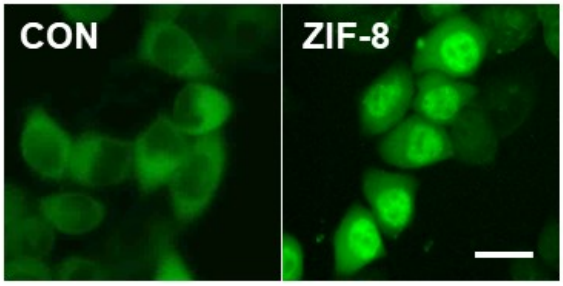

Figure S11. Representative images of GFP-TFEB in MCF-7 cells treatments with PBS (CON) or ZIF-8 for 6h. Scale bar: 20 μm.

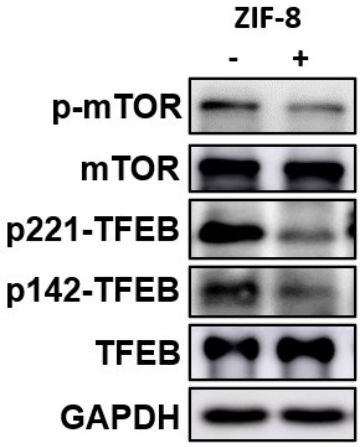

Figure S12. Western blotting analysis of MCF-7 with or without ZIF-8 treatment at 100 μg mL $^{-1}$ for 4 h and tested the level of phosphor-mTOR (Ser2448), total mTOR, phosphor-TFEB (Ser142), phosphor-TFEB (Ser211) and total TFEB repratively.

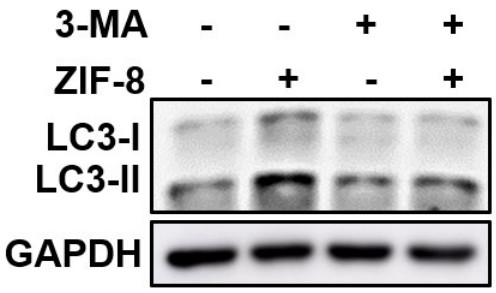

Figure S13. Western blotting analysis of the level of LC3 proteins in HeLa cells with treatments of PBS (CON) or 100 μg mL $^{-1}$ ZIF-8 in the presence of 3-MA or not for 10 h.

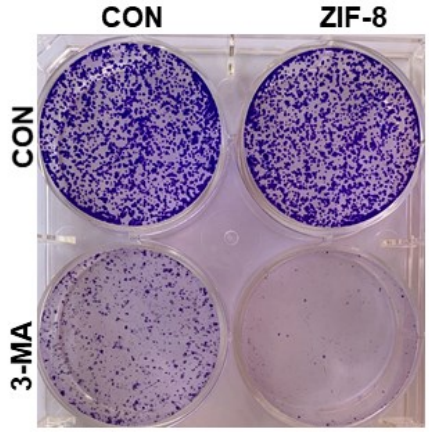

Figure S14. Clone formation of HeLa cells after treatments of PBS (CON) or 100 μg mL $^{-1}$ ZIF-8 with or without 3-MA for 24 h.

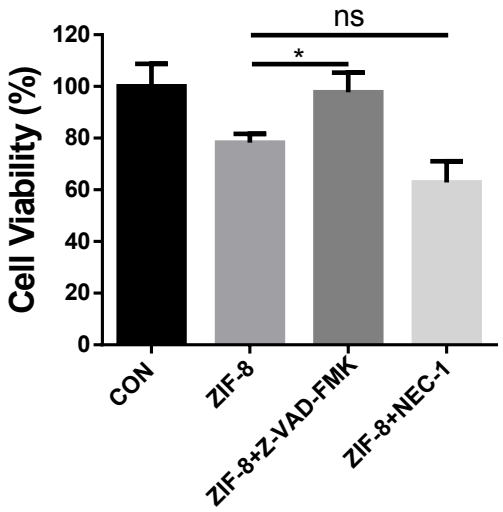

Figure S15. Cell viability of HeLa cells by MTT assay with treatments of PBS (CON), ZIF-8, ZIF-8+Z-VAD-FMK (selective apoptosis inhibitor), or ZIF-8+NEC-1 (specific necrosis inhibitor) for 10 h.

Figure S16. Western blotting of ATG5 and LC3 protein levels after transfecting negative control si-RNA (si-*NC*) or ATG5 si-RNA (si-*ATG5*) to HeLa cells for 36 h following PBS or ZIF-8 treatment.

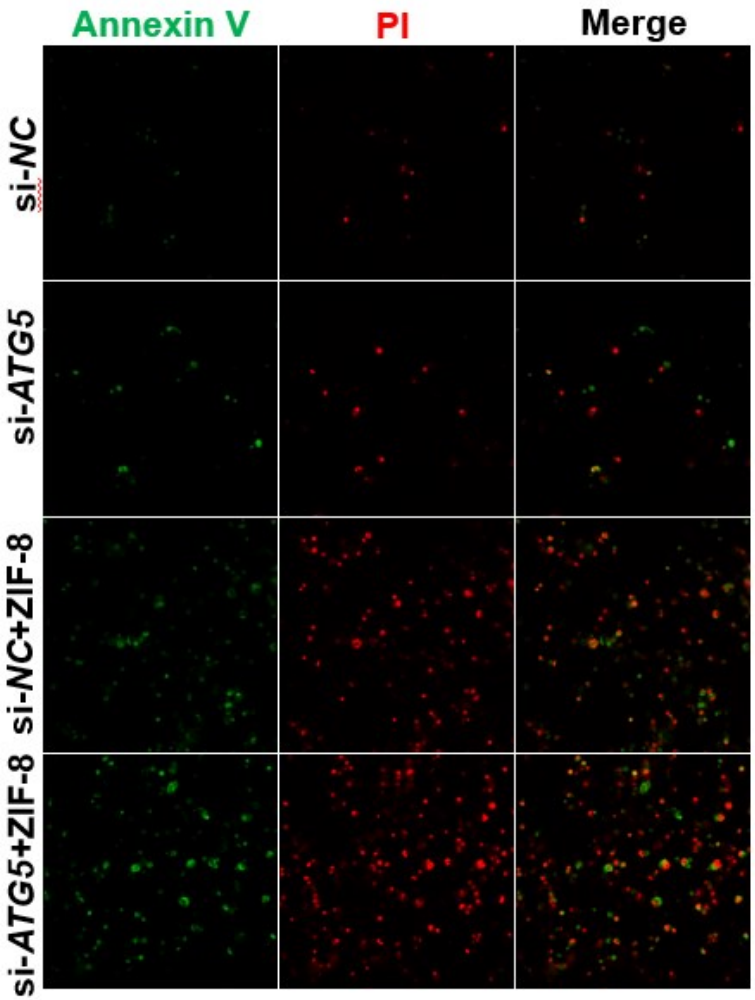

Figure S17. Cell viability of HeLa cells staining by Annexin-V/PI with 100 μg mL $^{-1}$ ZIF-8 for 10 h or not following knockdown assay with negative control siRNA (si-*NC*) or *ATG5* si-RNA (si-*ATG5*) for 36 h.

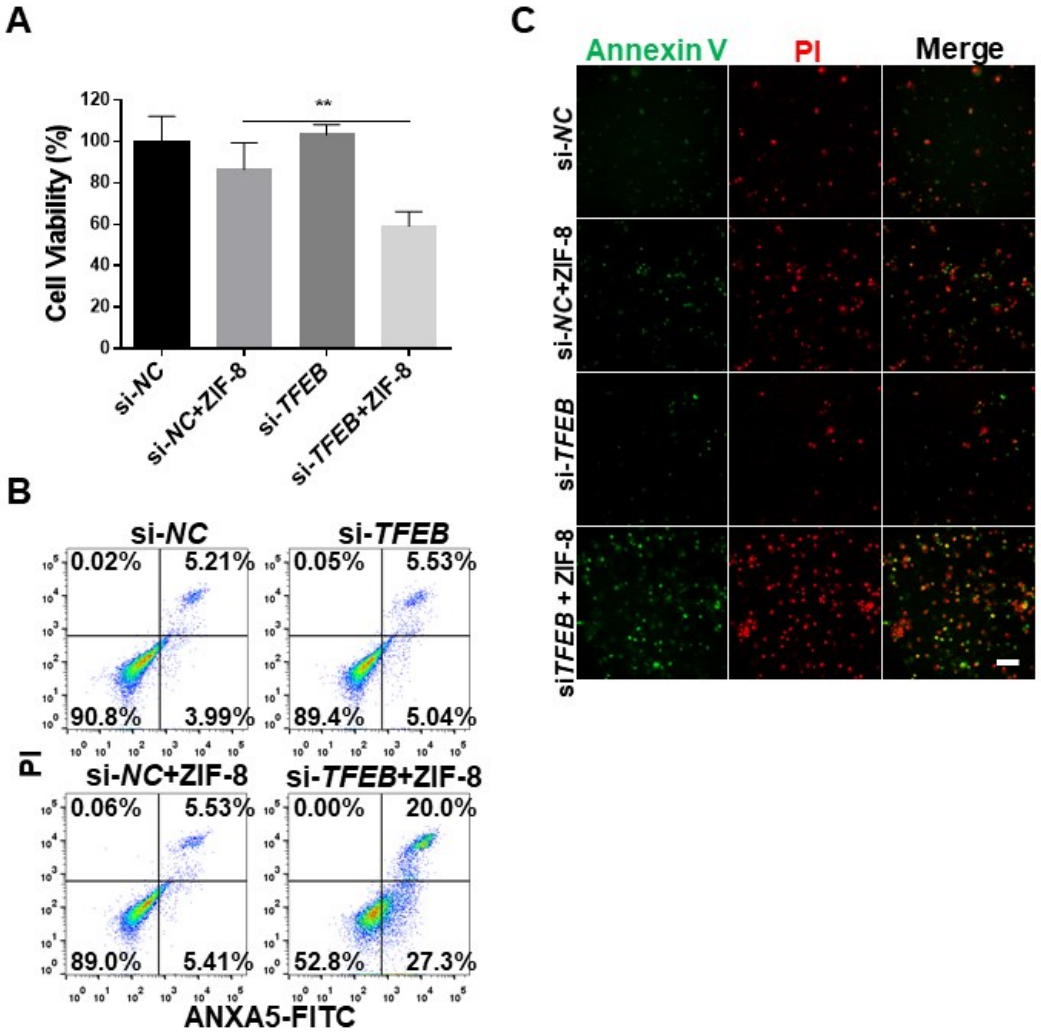

Figure S18. (A) Cell viability by MTT assay after treating HeLa cells with or without 100 μg mL $^{-1}$ ZIF-8 for 10 h following transfection with negative control si-RNA (si-*NC*) or *TFEB* si-RNA (si-*TFEB*) for 36h. (B, C) Flow cytometry analysis (B) and representative fluorescent images (C) of HeLa cells stained by Annexin-V/PI for 15 min after treatments of PBS (CON) or 100 μg mL $^{-1}$ ZIF-8 for 10 h, in the condition of transfecting negative control si-RNA (si-*NC*) or *TFEB* si-RNA (si-*TFEB*) for 36h. Scale bar: 100μm.

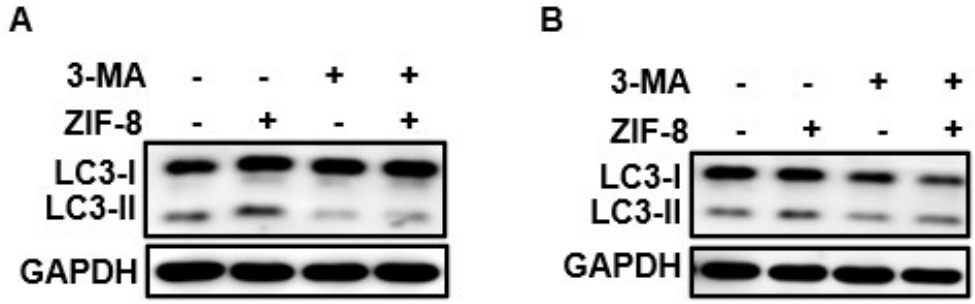

Figure S19. Western blotting analysis of the level of LC3 proteins in MCF-7 cells (A) and NCI-H1299 cells (B) with treatments of PBS (CON) or 50 μg mL $^{-1}$ ZIF-8 in the presence of 3-MA or not for 12 h.

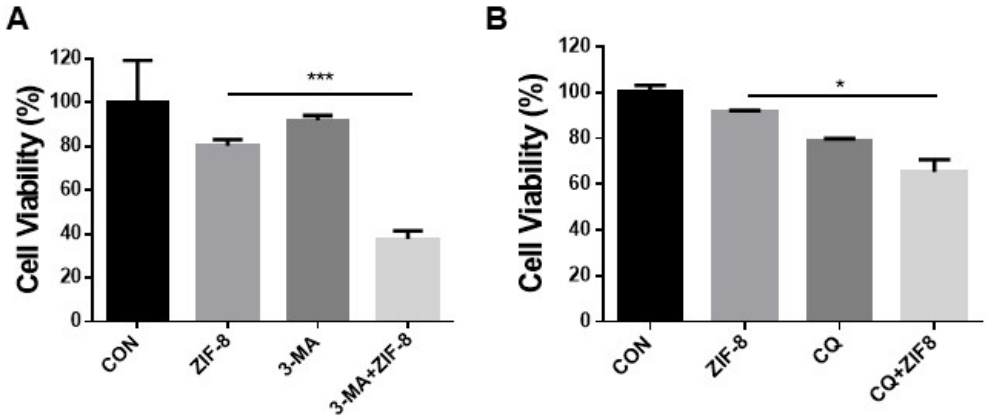

Figure S20. Cell viability of MCF-7 cells (A) or H1299 cells (B) by MTT assay after treating HeLa cells with or without 50 μg mL $^{-1}$ ZIF-8 and autophagy inhibitors (3-MA, or CQ) for 24 h.

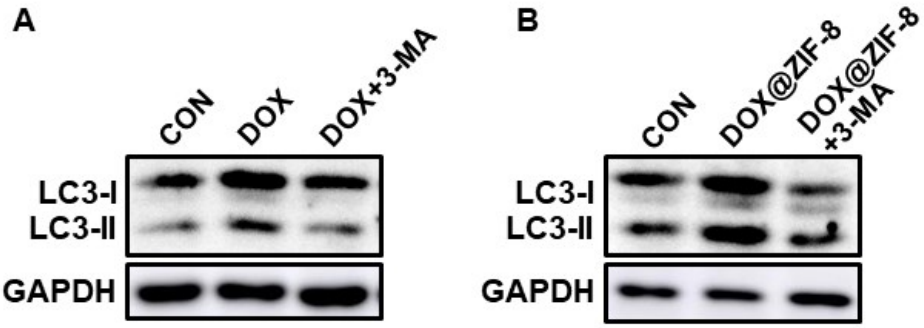

Figure S21. Western blotting analysis of the level of LC3 proteins in HeLa cells with treatments of PBS (CON), 1 μg mg $^{-1}$ DOX or DOX+3-MA for 24 h (A) and PBS (CON), DOX@ZIF-8 or DOX@ZIF-8 +3-MA for 24 h.

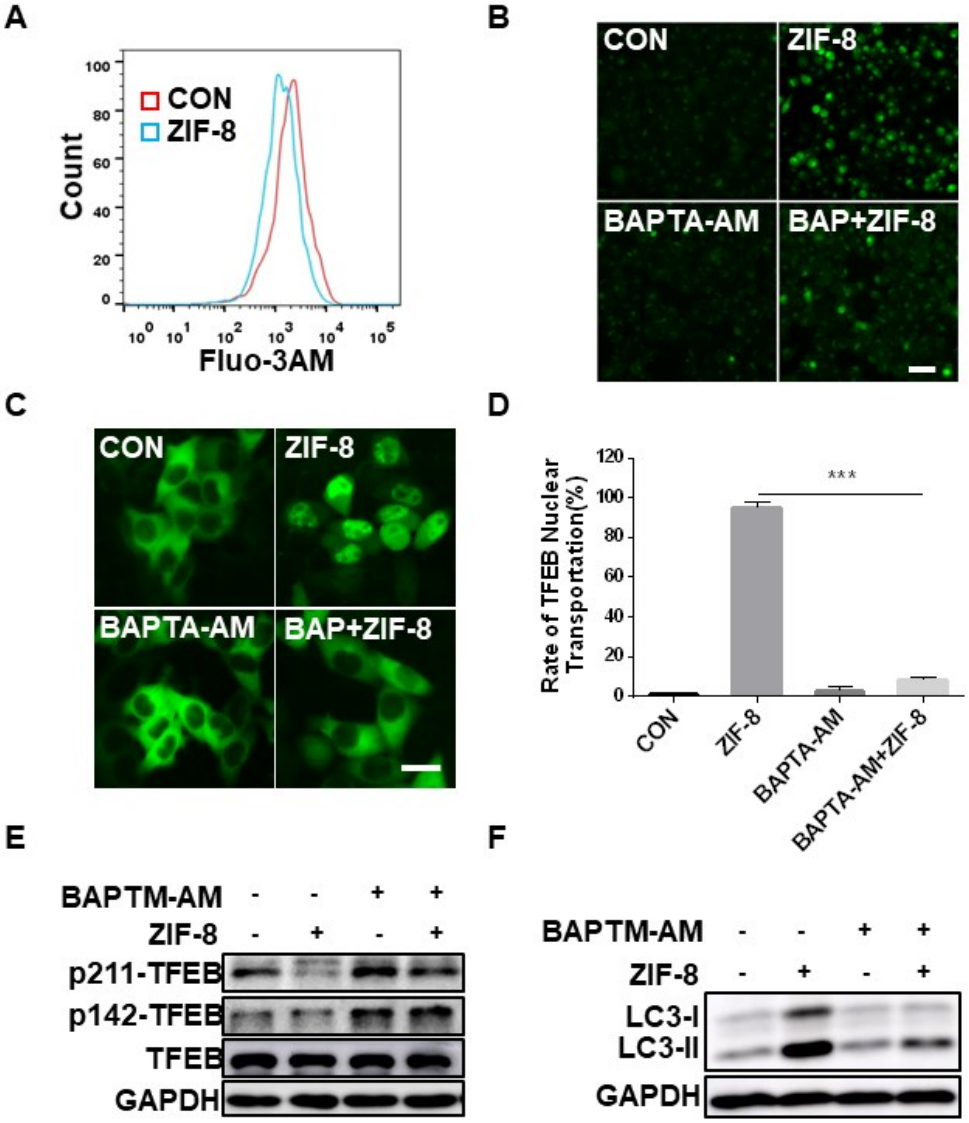

Figure S22. Ca^{2+} mobilization may play an important role in ZIF-8 induced TFEB activation. (A, B) Intracellular calcium detected by Fluo-3AM probe with PBS (CON) or 100 μg mL -1 ZIF-8 treatment by flow cytometry (A) and fluorescence images (B). BAPTA-AM: 10 μM. Scale bar: 50 μm. (C, D) Representative images (C) of HeLa EGFP-TFEB with PBS (CON) or 100 μg mL -1 ZIF-8 treatments for 6 h together with 10 μM BAPTA-AM or not. Scale bar: 20 μm. Quantified data in D was obtained by counting at least 300 cells each group. (E) Western blotting analysis of phosphor-TFEB (Ser142), phosphor-TFEB (Ser211) and total TFEB after treatments with PBS or 100 μg mL $^{-1}$ ZIF-8, in the presence or absence of 10 μM BAPTA-AM for 6 h in HeLa EGFP-TFEB cells.（F） Western blotting analysis of LC3 after treatments with PBS or 100 μg mL $^{-1}$ ZIF-8 for 10 h, with or without 10 μM BAPTA-AM in HeLa cells.

Table S1. RT-PCR Primer Sequences.

Gene Name	Forward primer sequence (5′-3′)	Reverse primer sequence (5′-3′)
MAPLC3B	GAGAAGCAGCTTCCTGTTCTGG	GTGTCCGTTCACCAACAGGAAG
SQSTM1	GCACCCCAATGTGATCTGC	CGCTACACAAGTCGTAGTCTGG
LAMP1	ACGTTACAGCGTCCAGCTCAT	TCTTTGGAGCTCGCATTGG
CTSB	AGTGGAGAATGGCACACCCTACTSD	AAGAAGCCATTGTCACCCCA
CTSD	AACTGCTGGACATCGCTTGCT	CATTCTTCACGTAGGTGCTGGA
ATP6V1H	GGAAGTGTCAGATGATCCCCA	CCGTTTGCCTCGTGGATAAT
VPS11	CAAGCCTACAAACTACGGGTG	GAGTGCAGAGTGGATTGCCA
VPS18	CAAGGCAAATGAGCCCAACC	GCTAGTGGCCGTACCTTCTG
ACTB	GATCATTGCTCCTCCTGAGC	ACTCCTGCTTGCTGATCCAC