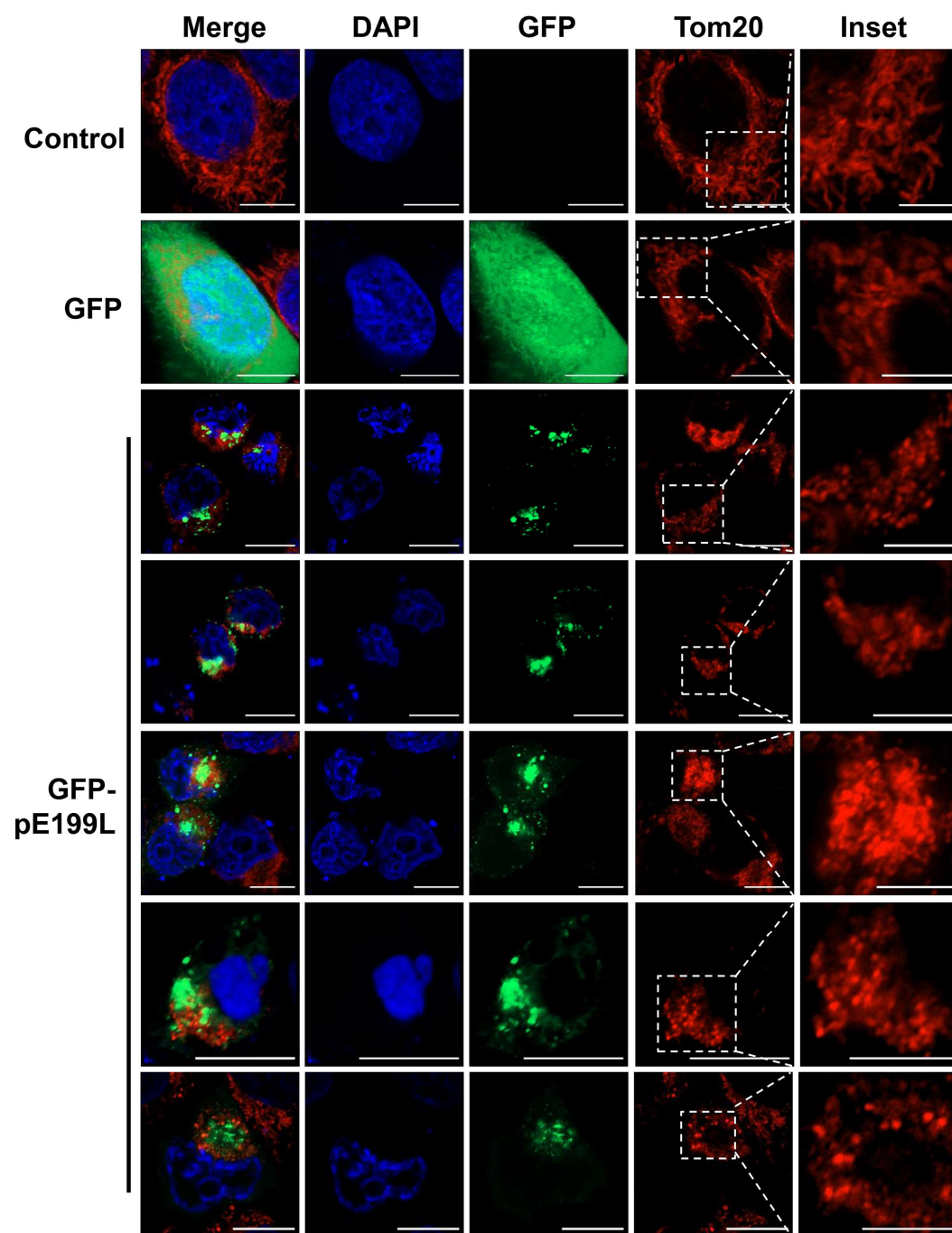
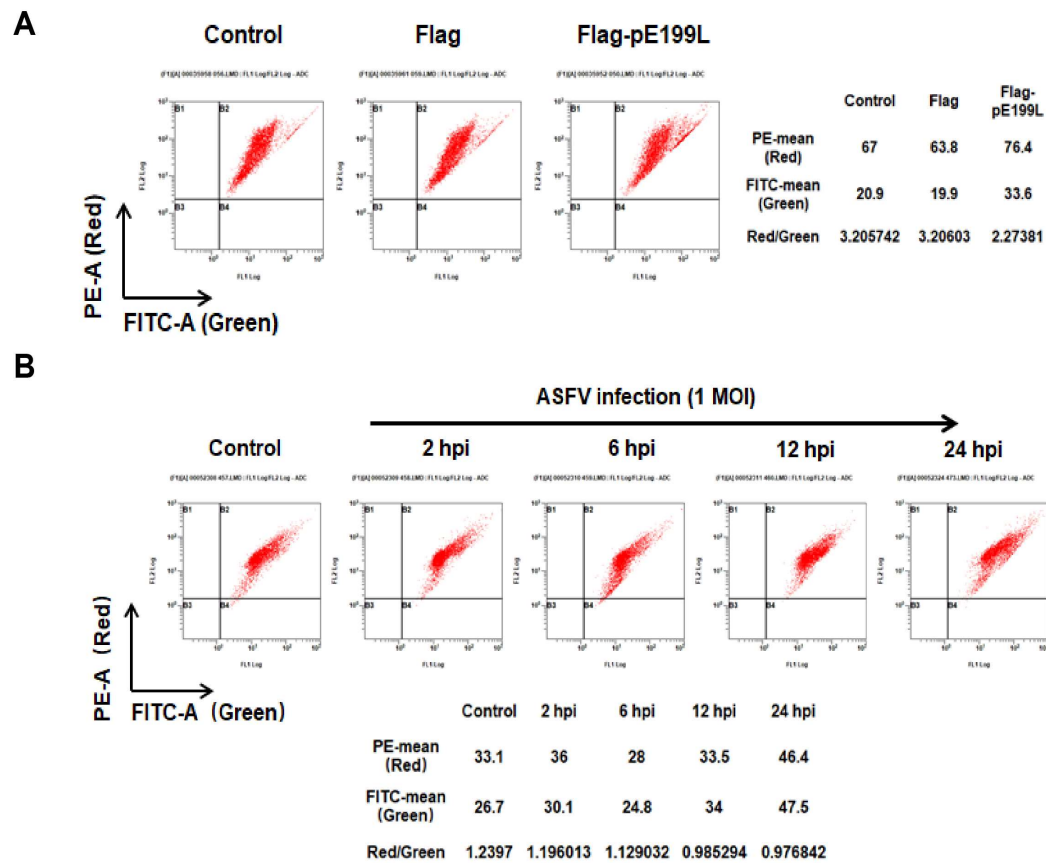


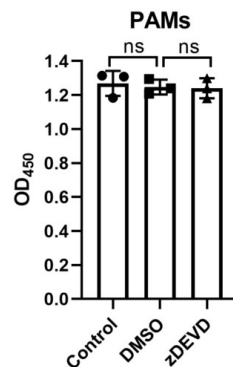
**Figure S1.** (A,B) Fluorescence images of PI-staining assay in GFP, GFP-pE199L or GFP-pE183L-expressing HEK293T (A) or CRL-2843 cells (B). HEK293T or CRL-2843 cells were transfected with pEGFP-C1, pGFP-E199L or pGFP-E183L plasmids for 36 h and then stained with PI for 15 min. Representative fluorescence images (left) were visualized using a fluorescence microscope (Invitrogen EVOS FL Auto 2.0) under a 20 $\times$  objective. Green, GFP, GFP-pE199L or GFP-pE183L; Red, PI; Scale bar, 125  $\mu$ m. The right panels showed the statistical analysis of the percentage of PI-labeling cells in GFP, GFP-pE199L or GFP-pE183L-expressing cells. PI-labeling cells from 10 fields (approximately 100 cells/ field) were counted under a 20 $\times$  objective and the results were shown as mean  $\pm$  SD values, n=30 from three independent experiments. The significance of the differences between the groups was determined by Brown-Forsythe and Welch ANOVA test with Dunnett T3 (A) or Mann-Whitney-test (B) (\*\*\*) indicates  $p < 0.001$ ).



**Figure S2.** Representative confocal images of morphology changes of the mitochondria induced by pE199L in HeLa cells under conditions outlined in Figure 4A. Insets scale bar, 5  $\mu\text{m}$  and others scale bar, 10  $\mu\text{m}$ .



**Figure S3.** (A) Representative dot blot images of the mitochondrial membrane potential assay in HeLa cells under conditions outlined in Figure 4C. (B) Representative dot blot images of the mitochondrial membrane potential assay in PAMs cells under conditions outlined in Figure 6A.



**Figure S4.** Detection of the cytotoxicity of z-DEVD-FMK on PAMs by WST-1 assay according to the manufacturer's instructions (Beyotime, China). PAMs were treated with z-DEVD-FMK at 200  $\mu$ M or an equal volume of DMSO for 48 h, and then the cultured medium was removed and subsequently WST-1 solution (1:10 dilution) was added. Cells were incubated at 37  $^{\circ}$ C for 1 h and analyzed at 450 nm on a microplate reader (SpectraMax iD3, Molecular Devices). Data are presented as the mean  $\pm$  SD,  $n = 3$ . The significance of the differences between the groups was determined by the Student's unpaired t-test with two tail (parametric test), ns indicates no statistically significant difference.