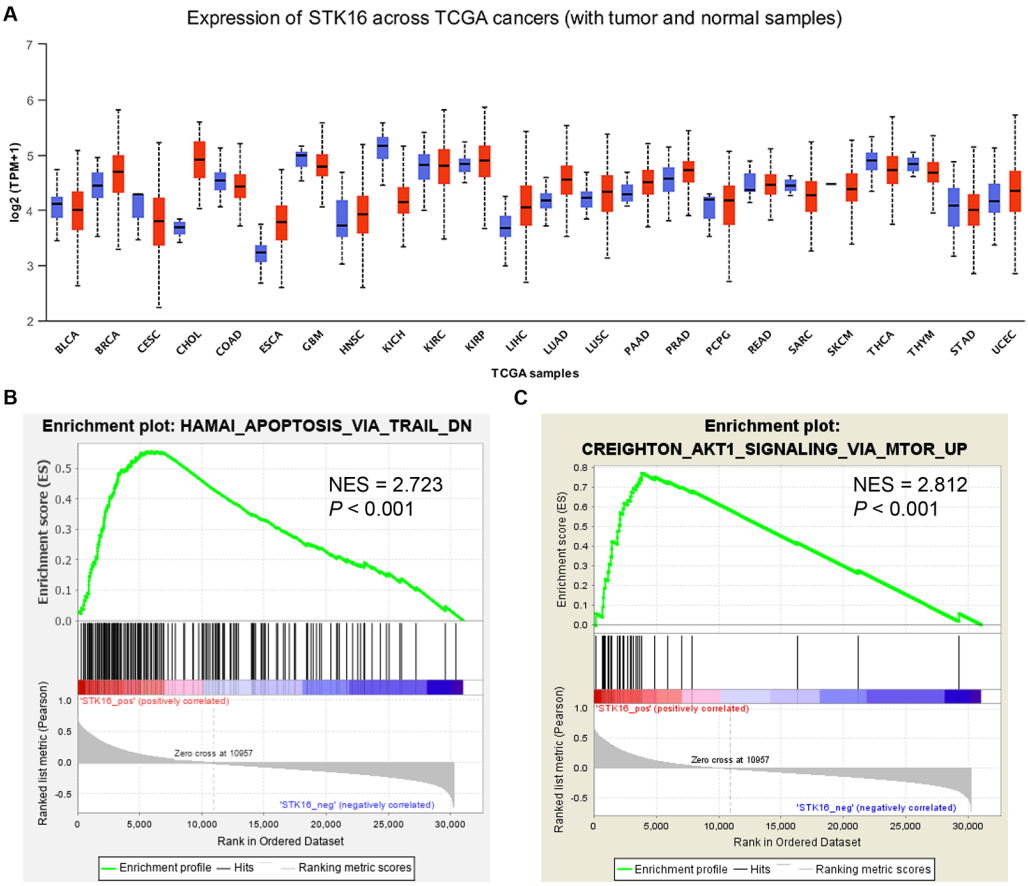

Figure S1. Bioinformatics analysis of STK16 expression in cancers and its correlation with signaling pathways. (A) The mRNA expression of STK16 was evaluated in patient samples from 24 TCGA projects. (B-C) GSEA demonstrated STK16 expression was associated with the Apoptosis and AKT1 signaling pathways.

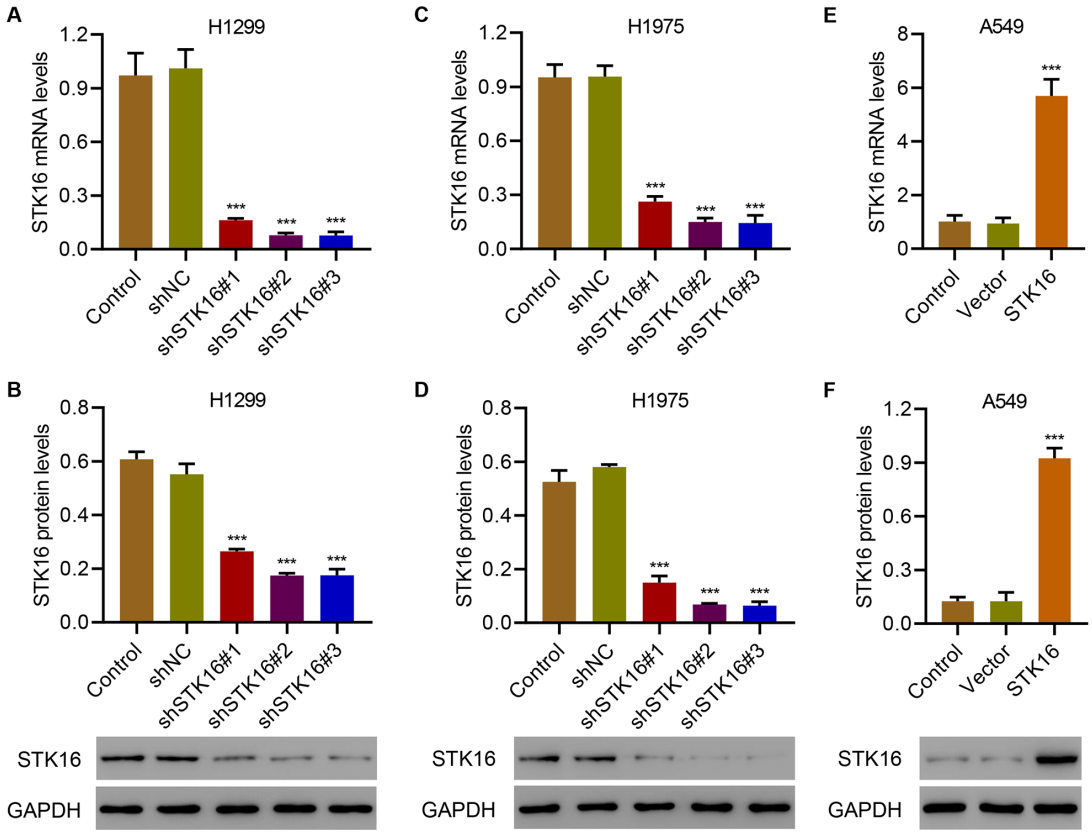

Figure S2. STK16 silencing and overexpression in LUAD cell lines. (A-D) STK16 expression in H1299 and H1975 cells transduced with STK16 shRNA vector. (E-F) STK16 expression in A549 cells transduced with STK16 expression vector. ***P<0.001 compared with shNC or vector.

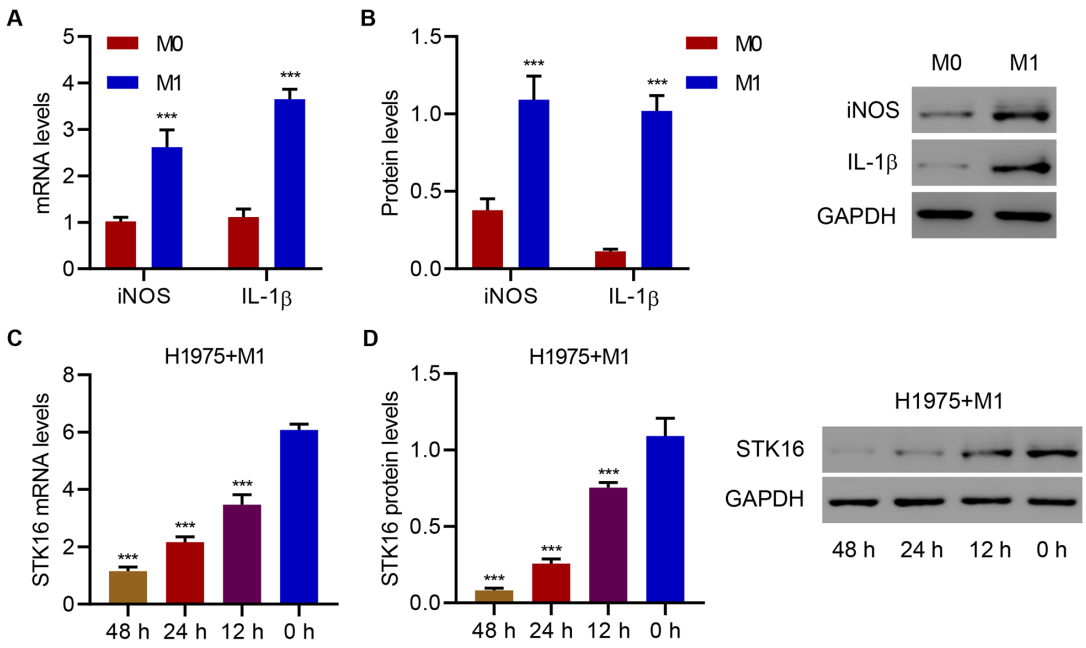

Figure S3. M1 macrophages inhibit STK16 expression. (A, B) Polarization of M1 macrophages was characterized by qRT-PCR and Western blotting of the markers. (D, D) STK16 expression in H1975 cells co-cultured with M1 macrophages was analyzed by qRT-PCR and Western blotting. ***P<0.001 compared with M0 or 0 h.

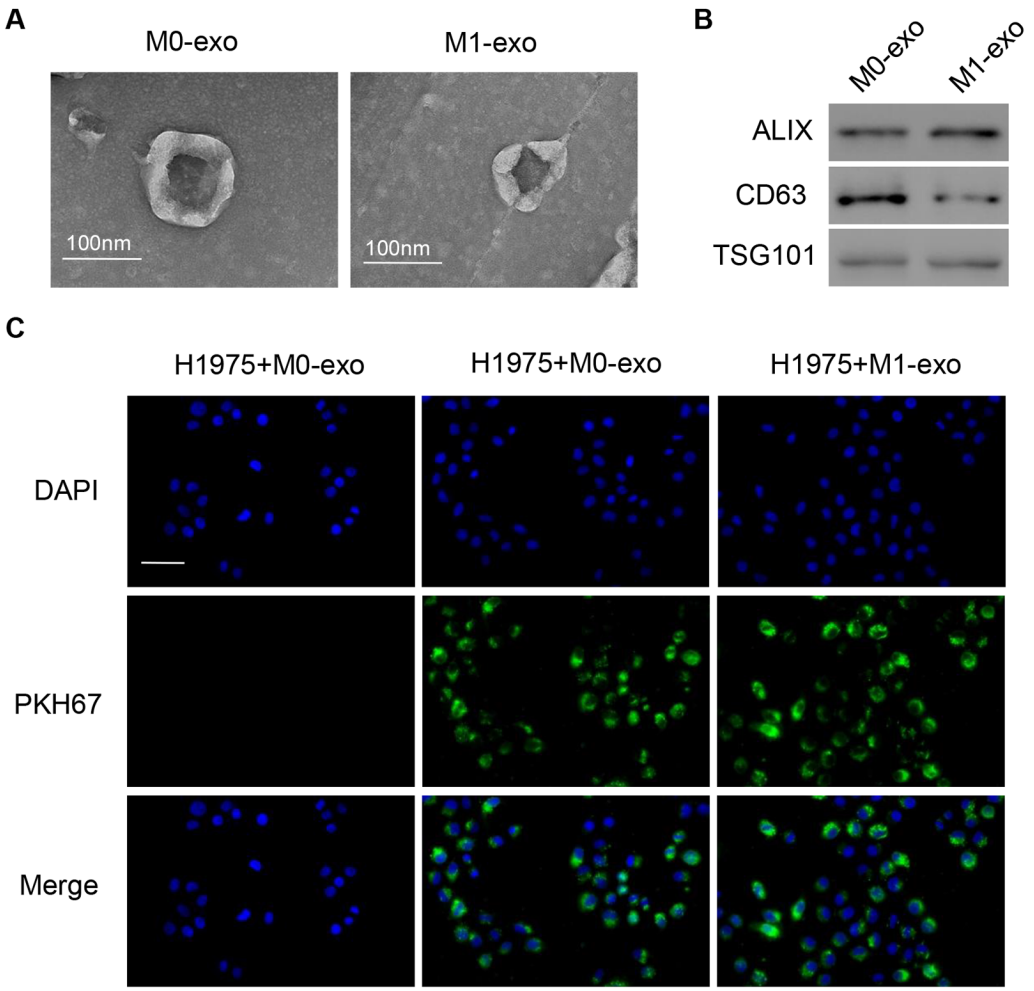

Figure S4. Characterization and internalization of exosome. (A) Electron microscopy image of exosome isolated from M0 and M1 macrophages. Scale bar = 100 nm. (B) Western blot analysis of ALIX, CD63, and TSG101 protein expression. (C) Internalization of exosomes by H1975 cells, visualized by laser scanning confocal microscope. Scale bar = 50 μm.

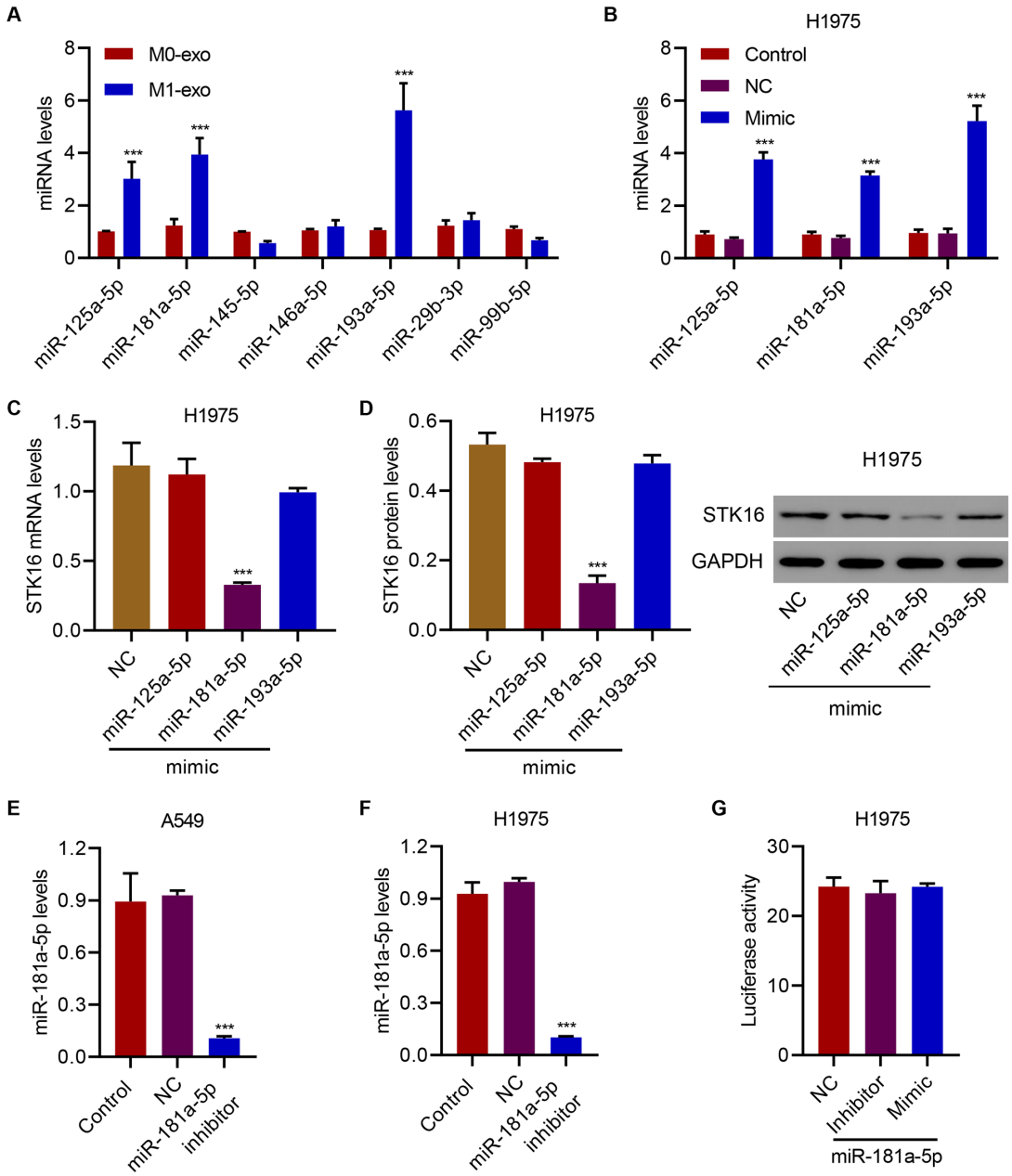

Figure S5. miR-181a-5p indirectly targets STK16. (A) Relative expression of miR-125a-5p, miR-181a-5p, miR-145-5p, miR-146a-5p, miR-193a-5p, miR-29b-3p, miR-99b-5p in exosome derived from M0 macrophages (M0-exo) or M1 macrophages (M1-exo). (B) Relative expression of miR-125a-5p, miR-181a-5p and miR-193a-5p in H1975 cells treated with miR-125a-5p, miR-181a-5p, or miR-193a-5p mimic, respectively. (C-D) Relative expression of STK16 in H1975 cells treated with miR-125a-5p, miR-181a-5p, or miR-193a-5p mimic, respectively. (E-F) Relative expression of miR-181a-5p in A549 and H1975 cells treated with miR-181a-5p inhibitor. ***P<0.001 compared with M0-exo or NC. (G) The luciferase activity of *STK16*

mRNA 3′UTR in H1975 cells transfected with miR-181a-5p mimic or inhibitor. ***P<0.001 compared with M0-exo or NC.

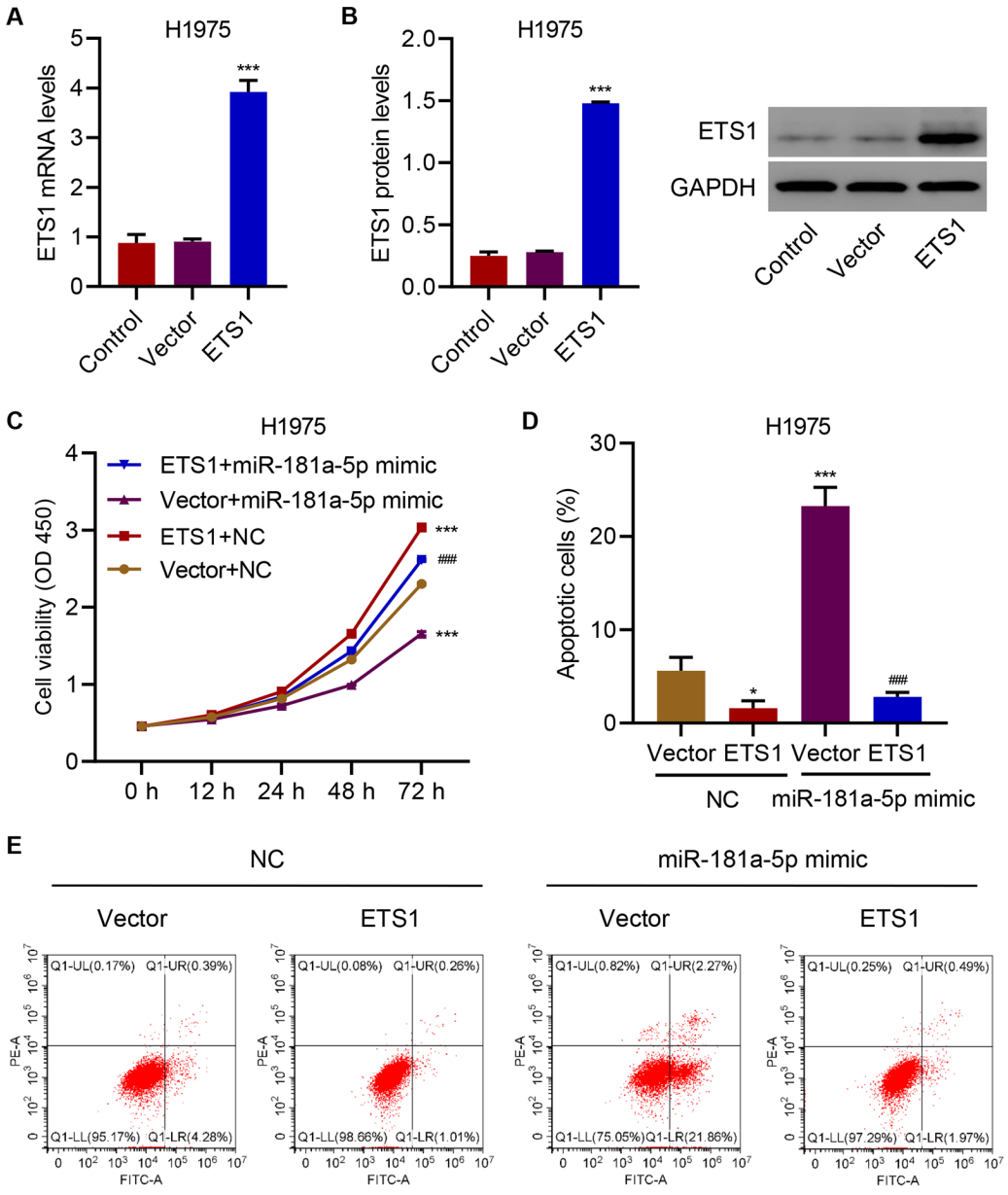

Figure S6. miR-181a-5p regulates cell viability and apoptosis by targeting ETS1. (A-B) ETS1 expression in H1975 cells transduced with ETS1 expression vector. (C) Cell viability and (D-E) apoptosis in H1975 cells transfected with miR-181a-5p mimic and transduced with ETS1 expression vector. ***P<0.001 compared with vector or vector+NC. $^{###}P$<0.001 compared with Vector+miR-181a-5p mimic.