Supplemental Figure 1

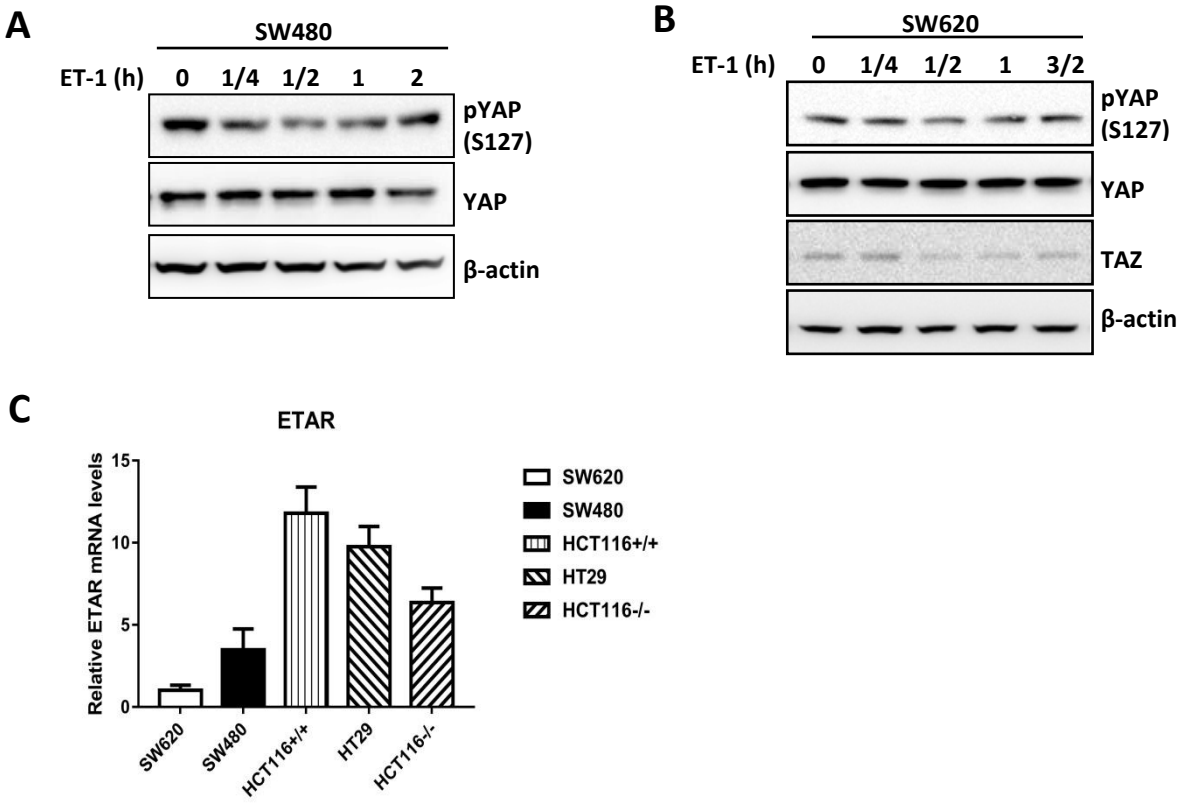

Figure S1. Stimulation of ETAR activates YAP/TAZ

(A) ETAR activation dephosphorylates YAP in SW480. SW480 cells were serum-starved for 14 h and treated with 150 nM of ET-1 for the duration indicated. (B) ET-1 is unable to induce YAP/TAZ dephosphorylation in SW620 cells. SW620 cells were serum-starved for 14 h and treated with 100 nM of ET-1 for the indicated times. (C) The response of YAP/TAZ to ET-1 is correlated to ETAR expression. mRNA expression level of ETAR in SW620, SW480, HCT116 $p53^{+/+}$, HT29 and HCT116 $p53^{-/-}$ cells were measured by Real-Time PCR.

Supplemental Figure 2

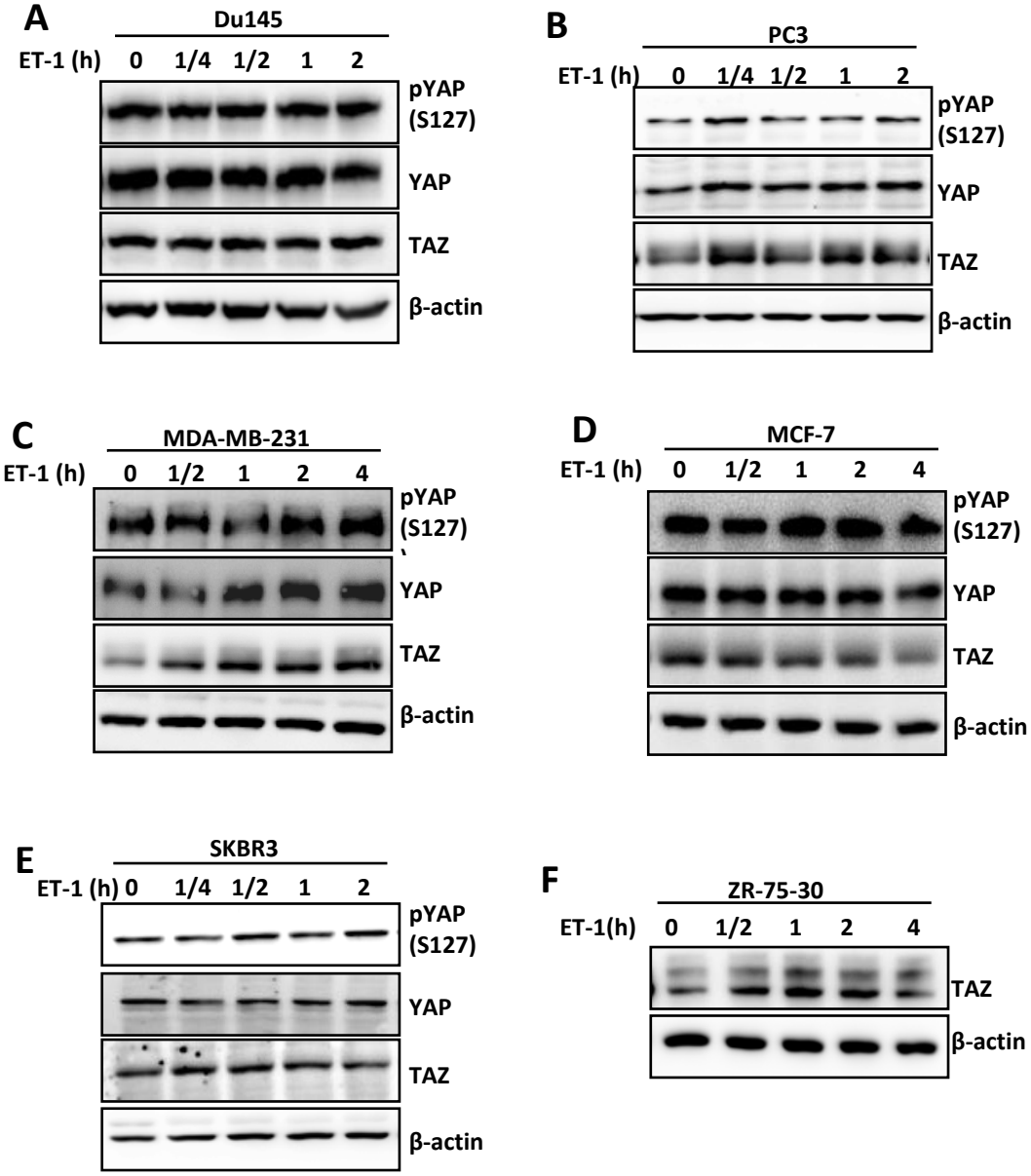

Figure S2. Effect of ET-1 on YAP/TAZ in prostate cancer cells and breast cancer cells

(A) ET-1 treatment in Du145 cells. Du145 cells were serum-starved for 14 h and treated with 100 nM of ET-1 for the duration indicated. (B) ET-1 treatment in PC3 cells. PC3 cells were serum-starved for 14 h and treated with 100 nM of ET-1 for the duration indicated. (C-F) Treatment of ET-1 in breast cancer cell lines. MDA-MB-231 (C), MCF7 (D), SKBR3 (E) and ZR-75-30 (F) cells were serum-starved for 14 h and treated with 100 nM of ET-1 for the duration indicated. ZR-75-30 cells show low expression of YAP protein.

Supplemental Figure 3

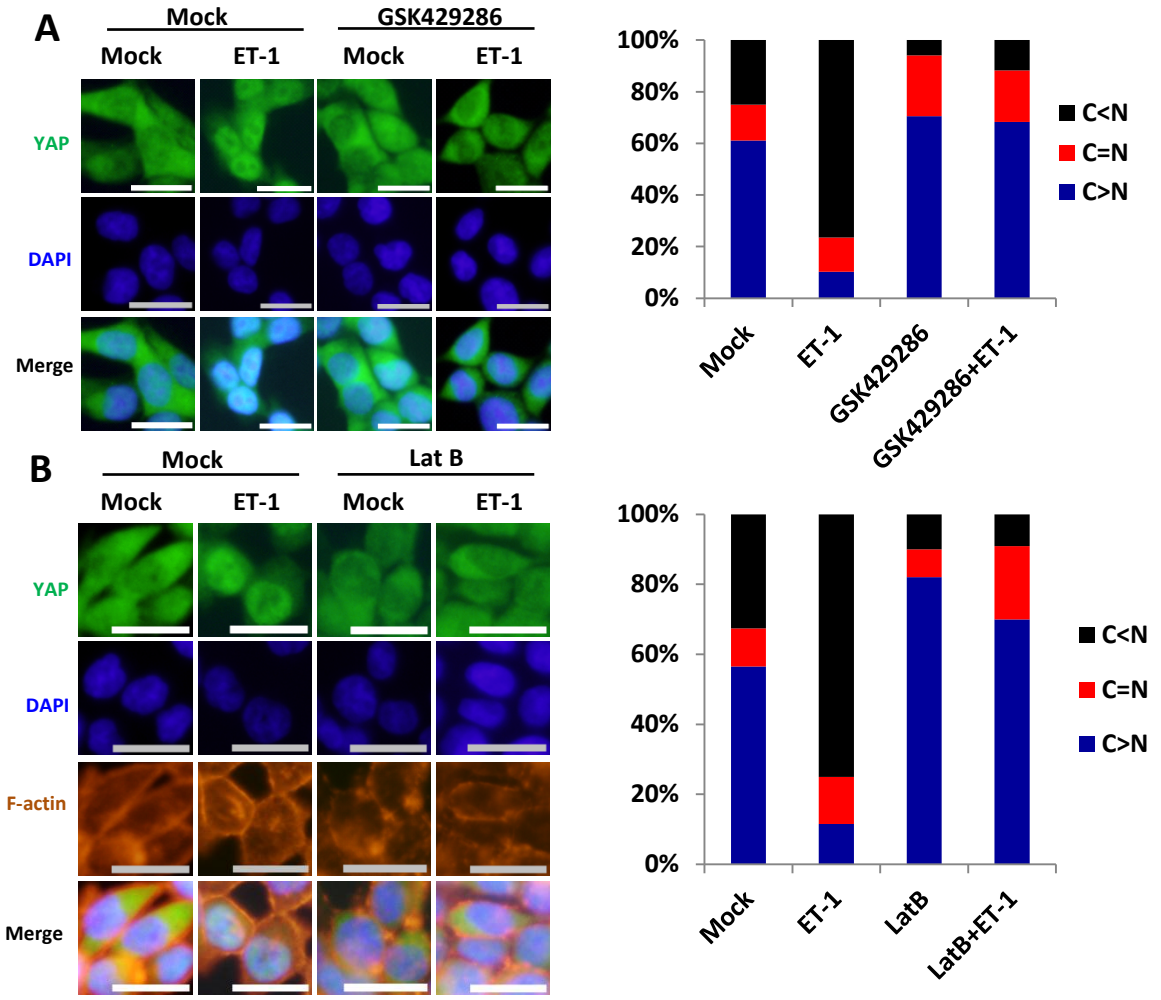

Figure S3. ET-1 acts through ROCK, actin cytoskeleton to stimulate YAP/TAZ

(A) ROCK is required for ET-1 induced YAP/TAZ nuclear translocation. Serum-starved HCT116 cells were pre-treated with GSK429286 (0.5 μM) for 4 h, and then were treated with 100 nM of ET-1 for 1 h. Endogenous YAP (green) and nuclei (blue) were stained with specific antibody and DAPI, respectively. Scale bar: 20 μm. Quantifications of YAP subcellular localization from at least 100 randomly selected cells was shown in the right panel. C, cytoplasm; N, nucleus. (B) Disruption of actin cytoskeleton blocks ET-1-induced YAP/TAZ nuclear translocation. Serum-starved HCT116 cells were pre-treated with latrunculin B (Lat B) (1 μg/ml) for 4 h, and then were treated with 100 nM of ET-1 for 1 h. Endogenous YAP (green) and nuclei (blue) were stained with specific antibody and DAPI, respectively. Scale bar: 20 μm. Quantifications of YAP subcellular localization from at least 100 randomly selected cells was shown in the right panel. C, cytoplasm; N, nucleus.

Supplemental Figure 4

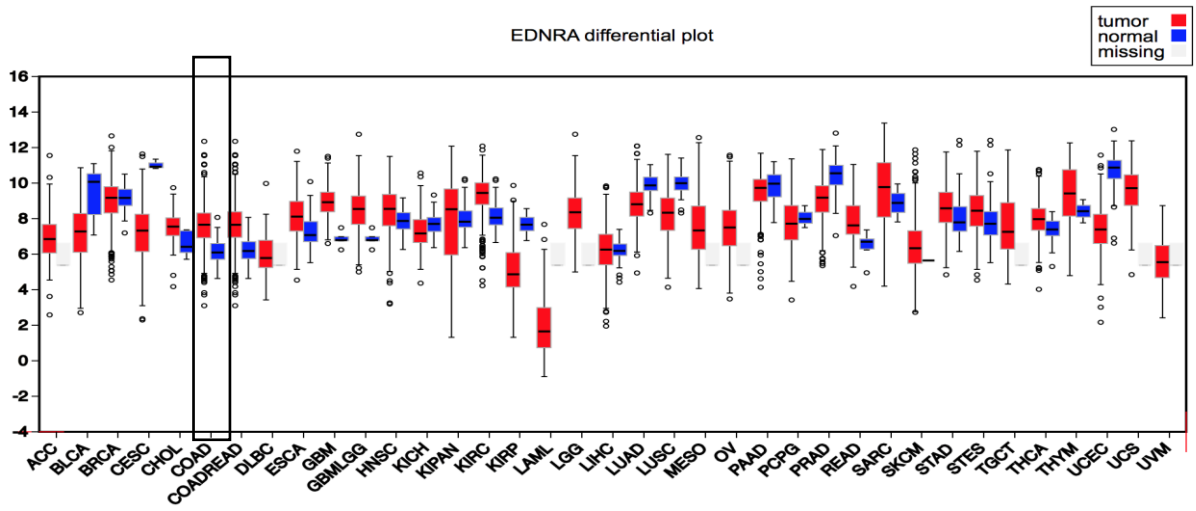

Figure S4. Expression levels of ETAR in tumors

(A) ETAR mRNA expression levels in various cancers. The differential plot of mRNA levels was drawn with FIREBROWSE shows in log2 RSEM. Expression of ETAR in colon cancers is boxed.