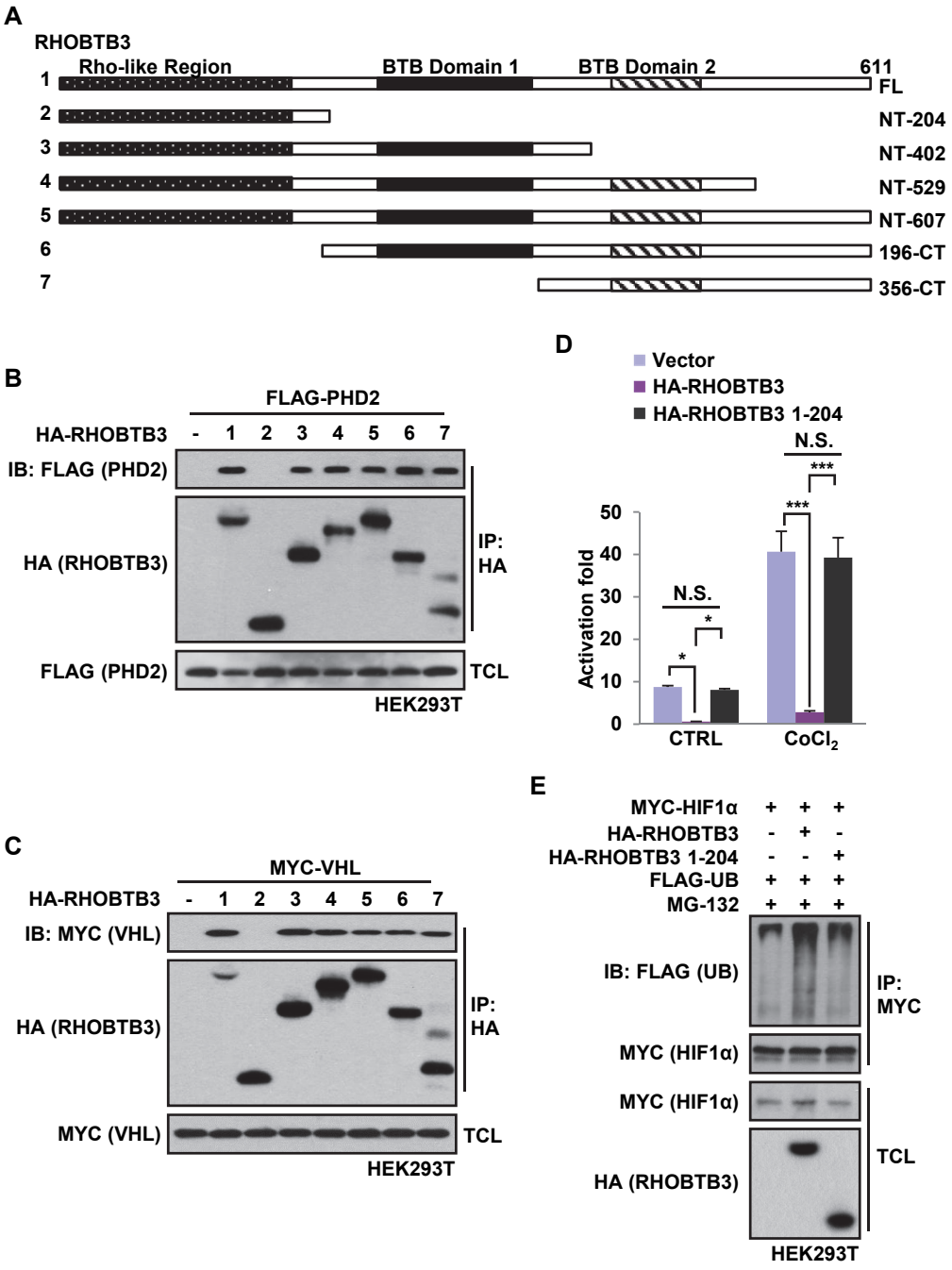

Supplementary information, Figure S4

(**A**) Schematic diagrams represent the full-length RHOBTB3 protein and its different deletion mutants used in the domain mapping experiments.

(**B, C**) RHOBTB3 interacts with PHD2 (**B**) and VHL (**C**) through its C terminus. FLAG-PHD2 (**B**) or MYC-VHL (**C**) was co-transfected with the blank vector pCMV-HA, different HA-tagged full-length RHOBTB3 or its deletion mutants into HEK293T cells. Cell lysates were immunoprecipitated using anti-HA antibody. Immunoprecipitates were analyzed by immunoblotting with antibodies indicated.

(**D**) The N-terminal region of RHOBTB3 (aa 1-204) has no effect on the transcriptional activity of HIF1α. *RHOBTB3*$^{-/-}$ MEFs were infected with lentiviruses expressing HA-RHOBTB3 or HA-RHOBTB3 (aa 1-204). At 36 h post-infection, cells were treated with $CoCl_2$ for 8 h and the transcriptional activities in the cell lysates were determined as described in Figure 2E. Data are presented as mean ± SEM, n = 3 for each group, *p < 0.01, ***p < 0.001 (ANOVA followed by Tukey). N.S., not significant.

(**E**) The N-terminal region of RHOBTB3 (aa 1-204) does not enhance the ubiquitination of HIF1α. HEK293T cells were transfected with indicated combinations of MYC-HIF1α, HA-RHOBTB3, HA-RHOBTB3 (aa 1-204) and FLAG-ubiquitin (UB). At 8 h post-transfection, cells were treated with 10 μM MG-132 for 10 h, followed by IP and analyzed as described in Figure 2G.