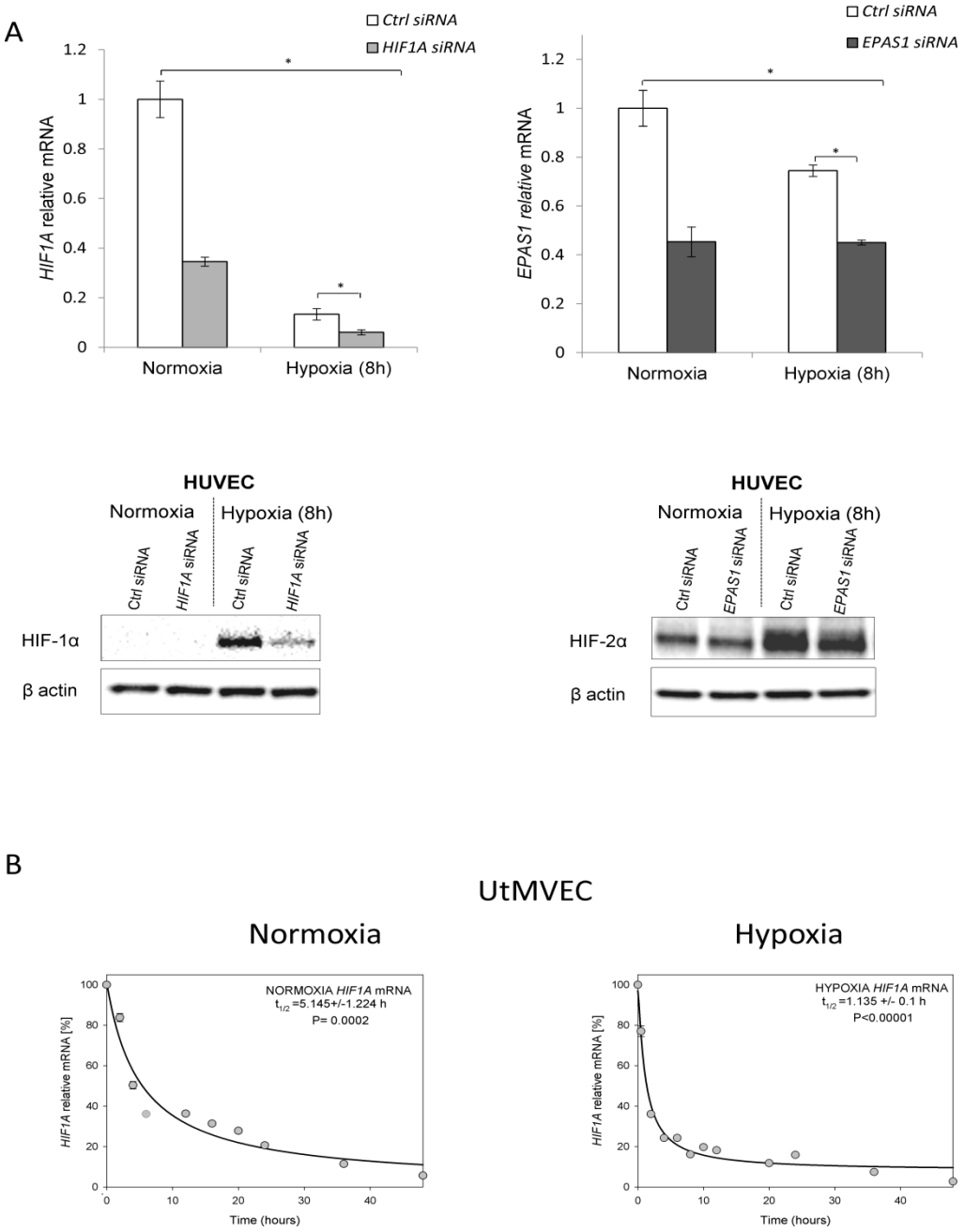

Supplemental Figure 2. *(A) siRNA-dependent HIF1A and EPAS1 mRNA degradation during hypoxia leads to lower HIF-1α and HIF-2α protein levels*. Following transfection with specific siRNA, HUVEC cells were exposed to hypoxia for 8 hours and total RNA and protein lysates were collected. The changes in HIF-1α and HIF-2α protein levels were evaluated by western blot normalized to β-actin and total protein levels and related to the normoxic siRNA control. *HIF1A* and *EPAS1* mRNA levels were quantified by qRT-PCR and normalized to *TBP* and *18S* rRNA levels and expressed as a fold change over normoxic samples. Data represent the mean ± SD of two independent experiments (3 replicates each). *P < 0.05 was considered significant. siRNA against *HIF1A* (Ambion assay id s6539) and *EPAS1* (Ambion assay id s4698) were purchased from Ambion. HUVEC cells were transfected using the Lipofectamine RNAiMax (Invitrogen, 13778030) according to manufacturer's protocol. The siRNAs were used at final concentrations of 40 nM. The transfected cells were cultured for 2 days prior to further analysis. Ambion siRNA Negative Control 1 (Ambion assay id MC22484) was used as a control. *(B) Hypoxia reduces mRNA levels and mRNA half-life of HIF1A in UtMVEC cells. HIF1A* and *EPAS1* mRNA

half-lives were monitored in UtMVECs exposed to hypoxia and cultured in normoxia. Actinomycin D was added to stop transcription, after which the RNA was isolated and total *HIF1A* mRNA levels at each time point were measured by RT-PCR and normalized to endogenous *18S* rRNA levels. mRNA values for each time point were calculated from two individual samples generated in at least two independent experiments. Relative *HIF1A* mRNA levels at the time points indicated were plotted as percent differences from *HIF1A* and *EPAS1* mRNA levels at the initial time point (t = 0). The mRNA half-lives were calculated from the exponential decay using the trend line equation $C/C_0 = e^{-kdt}$ (where C and C_0 are mRNA amounts at time t and at the t_0, respectively, and k_d is the mRNA decay constant). Results represent the mean ± SD of three measurements, * $P < 0.05$ was considered significant. The error bars represent SD.