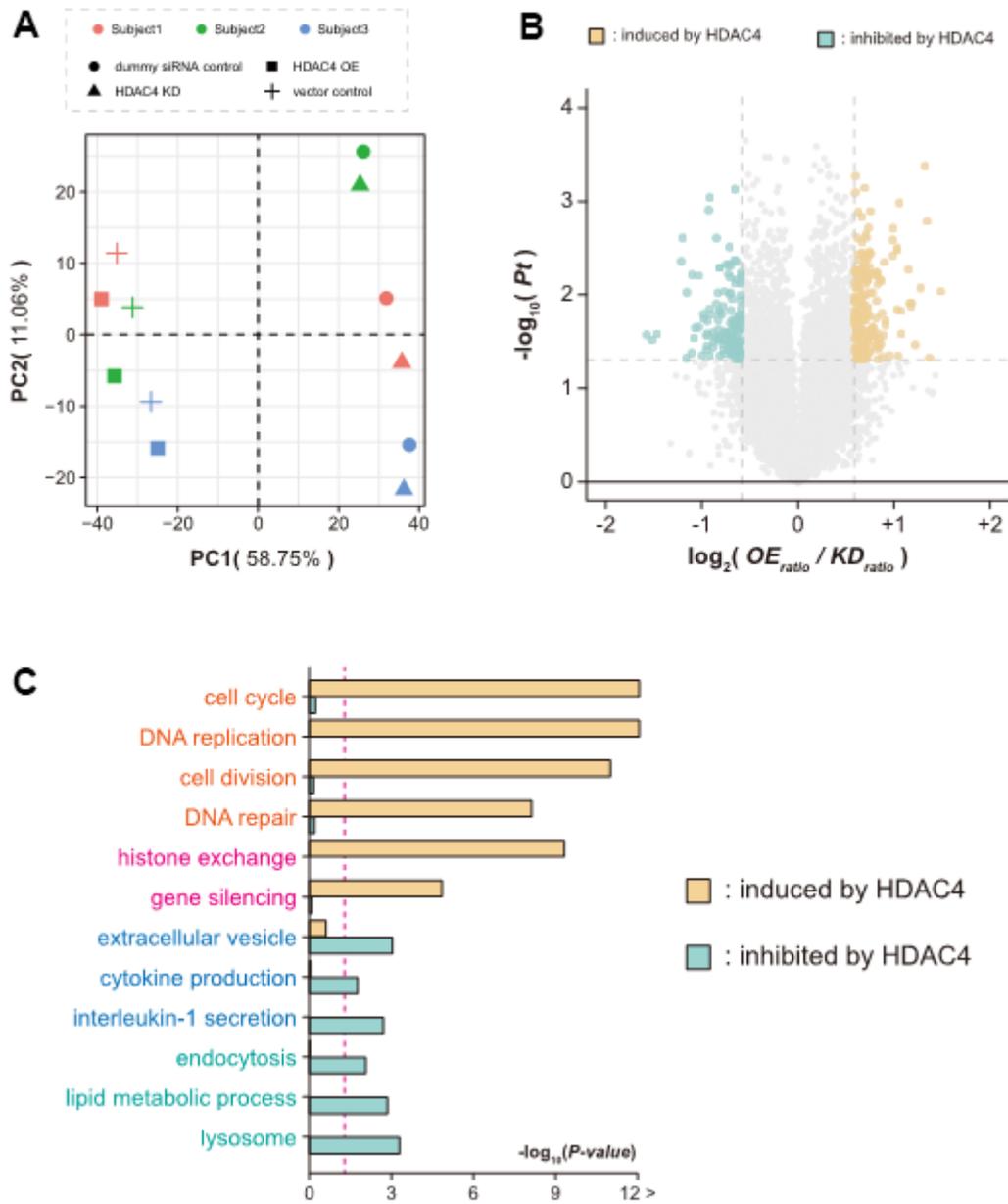
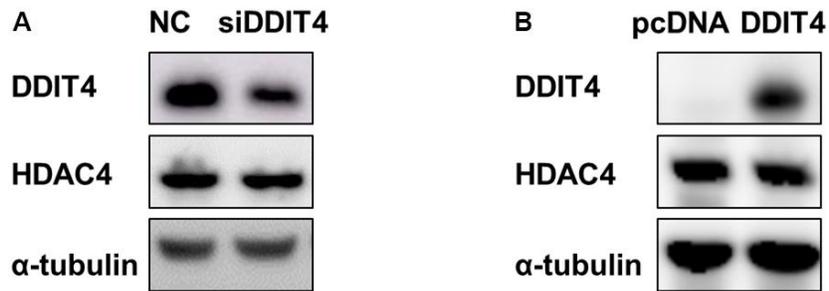


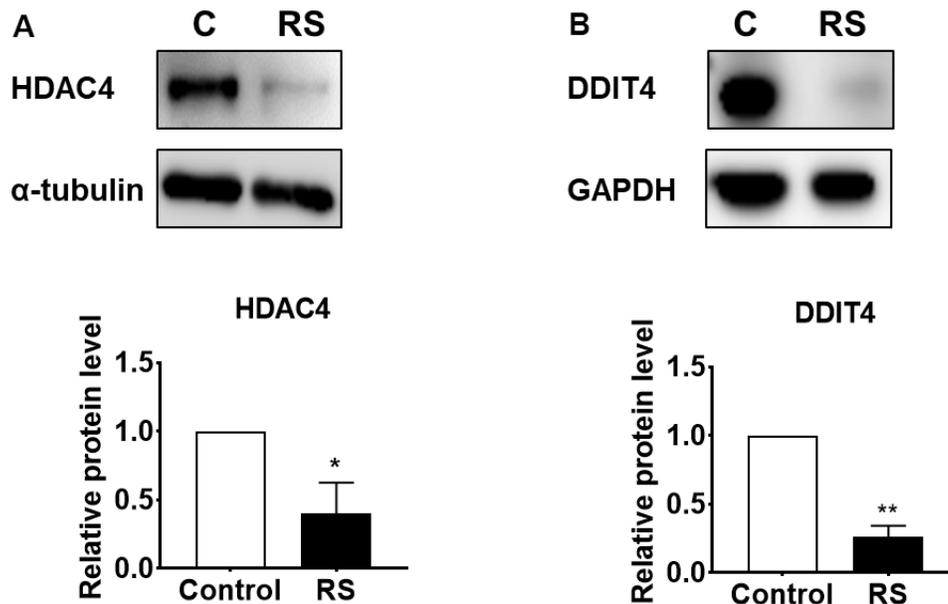
SUPPLEMENTARY FIGURES



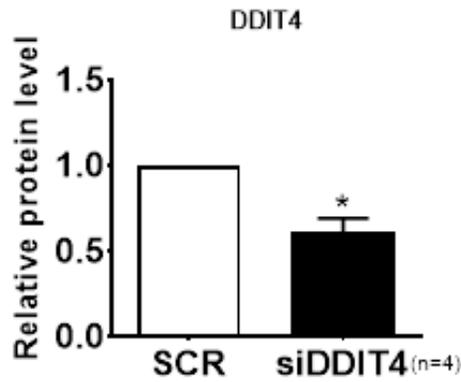
Supplementary Figure 1. Transcriptome analysis of HDAC4 modulated human dermal fibroblasts (HDFs). (A) Principle component analysis (PCA) plot showing the distribution of each sample. (B) Volcano plots displaying differentially expressed genes (DEGs) between OE_{ratio} (HDAC4 overexpression/vector control) and KD_{ratio} (HDAC4 knockdown/siRNA control) in HDFs. Green and yellow dots represent DEGs that are inhibited or induced by HDAC4, respectively. (C) Bar plot showing enrichment of cellular processes by DEGs. Red line represents the *P*-value cutoff (*P*=0.05).



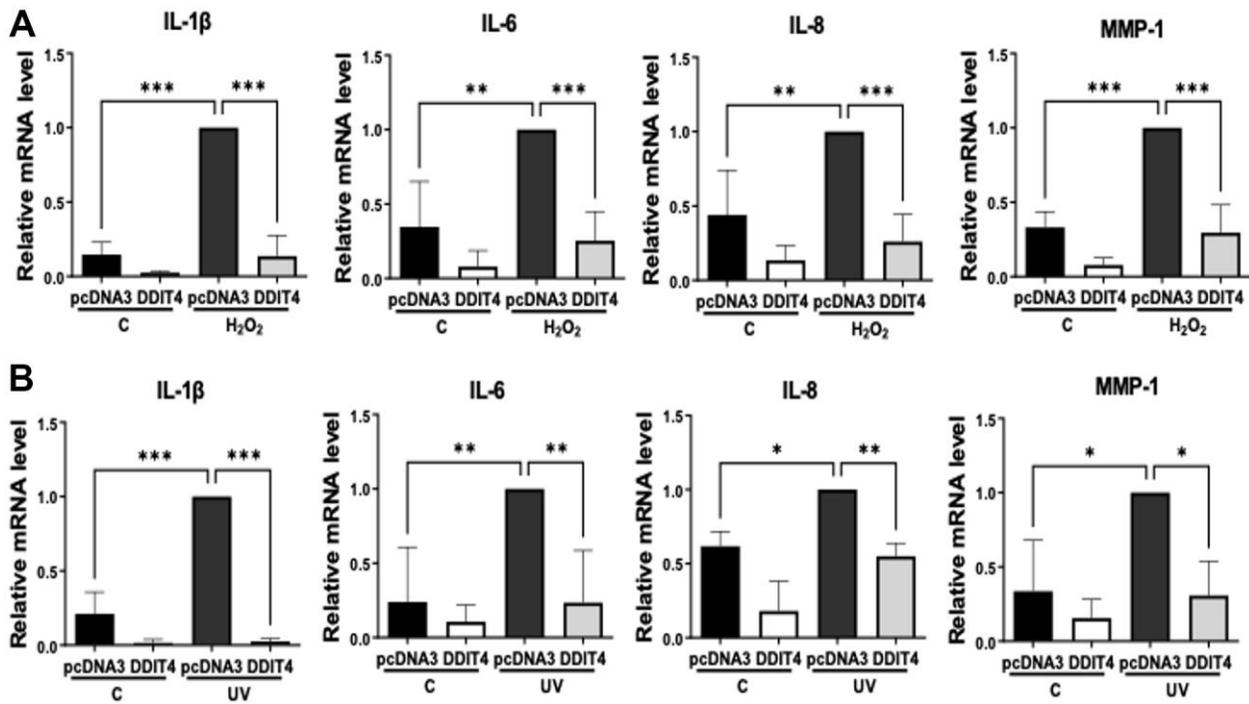
Supplementary Figure 2. DDIT4 does not change the expression of HDAC4. (A) Human dermal fibroblasts were transfected with negative control scrambled siRNA (NC) or DDIT4 siRNA (siDDIT4) (n=3). (B) For overexpression of DDIT4, cells were treated with pcDNA3 or DDIT4 plasmid DNA and the medium was replaced after 6 h (n=3). NC: scrambled control.



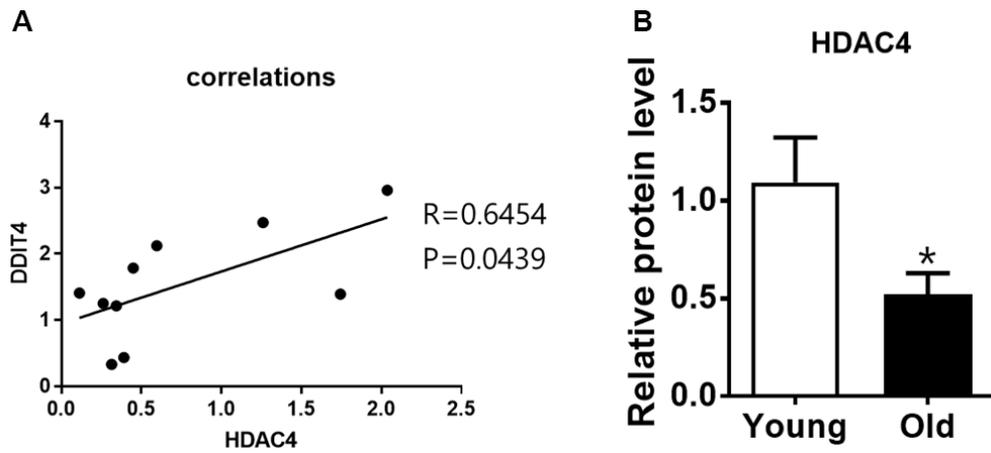
Supplementary Figure 3. Replicative senescent human dermal fibroblasts (HDFs) showed a decreased expression of HDAC4 and DDIT4 protein. (A, B) Low passage HDFs (passage 5-6) were continually cultured until replicative senescence (passage 40-45). The protein levels of HDAC4 and DDIT4 were analyzed by western blotting (n=4). Alpha-tubulin was used as a loading control. Data represent the mean \pm SE (n = 4, * P < 0.05, ** P < 0.01). Control: low-passage HDFs, RS: replicative senescent HDFs.



Supplementary Figure 4. The protein level of DDIT4 silenced by siDDIT4. Human dermal fibroblasts were transfected with negative control scrambled siRNA (NC) or DDIT4 siRNA (siDDIT4) (n=4). The protein level of DDIT4 was analyzed by western blotting. Data represent the mean \pm SE (*P<0.05).



Supplementary Figure 5. DDIT4 regulates the expression of senescence-associated secretory phenotype (SASP) in senescent cells induced by H₂O₂ or UV. The mRNA levels of SASP components (IL-1 β , IL-6, IL-8, and MMP-1) in human dermal fibroblasts induced by (A) H₂O₂ or (B) UV were determined by quantitative real-time PCR. Data represent the mean \pm SE (n = 3-4, *P<0.05, ** P <0.01, *** P <0.001).



Supplementary Figure 6. HDAC4 and DDIT4 has a positive correlation in young and aged skin. (A) Correlation test was performed to evaluate the association between DDIT4 and HDAC4 (n=10) (B) The protein level of HDAC4 in skin tissues from young (n=5) and elderly (n=5) subjects. Data represent the mean \pm SE (* P <0.05).