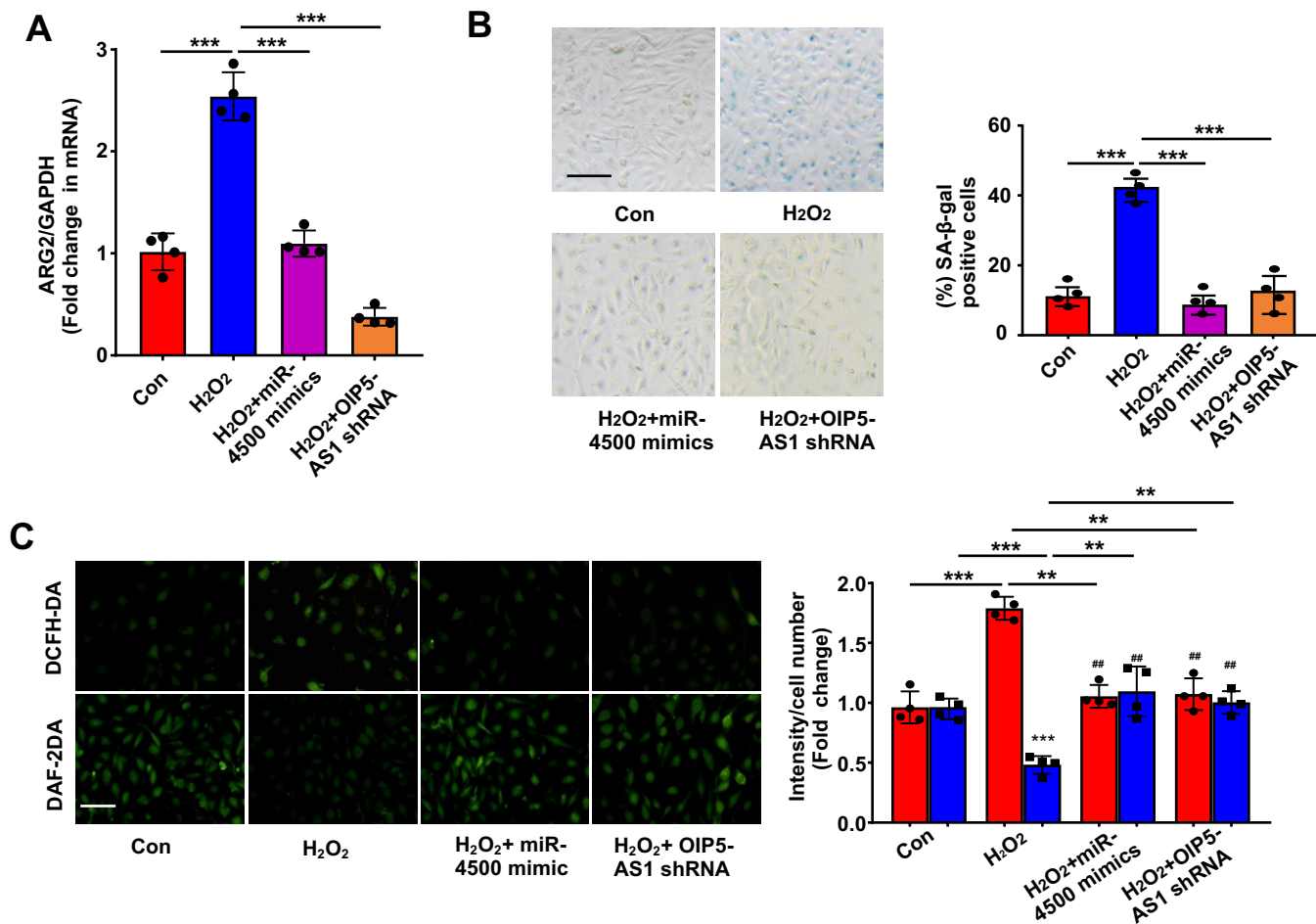
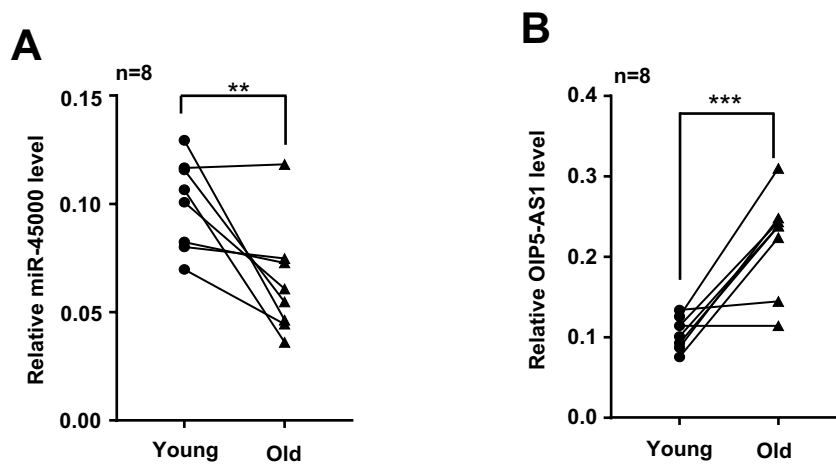


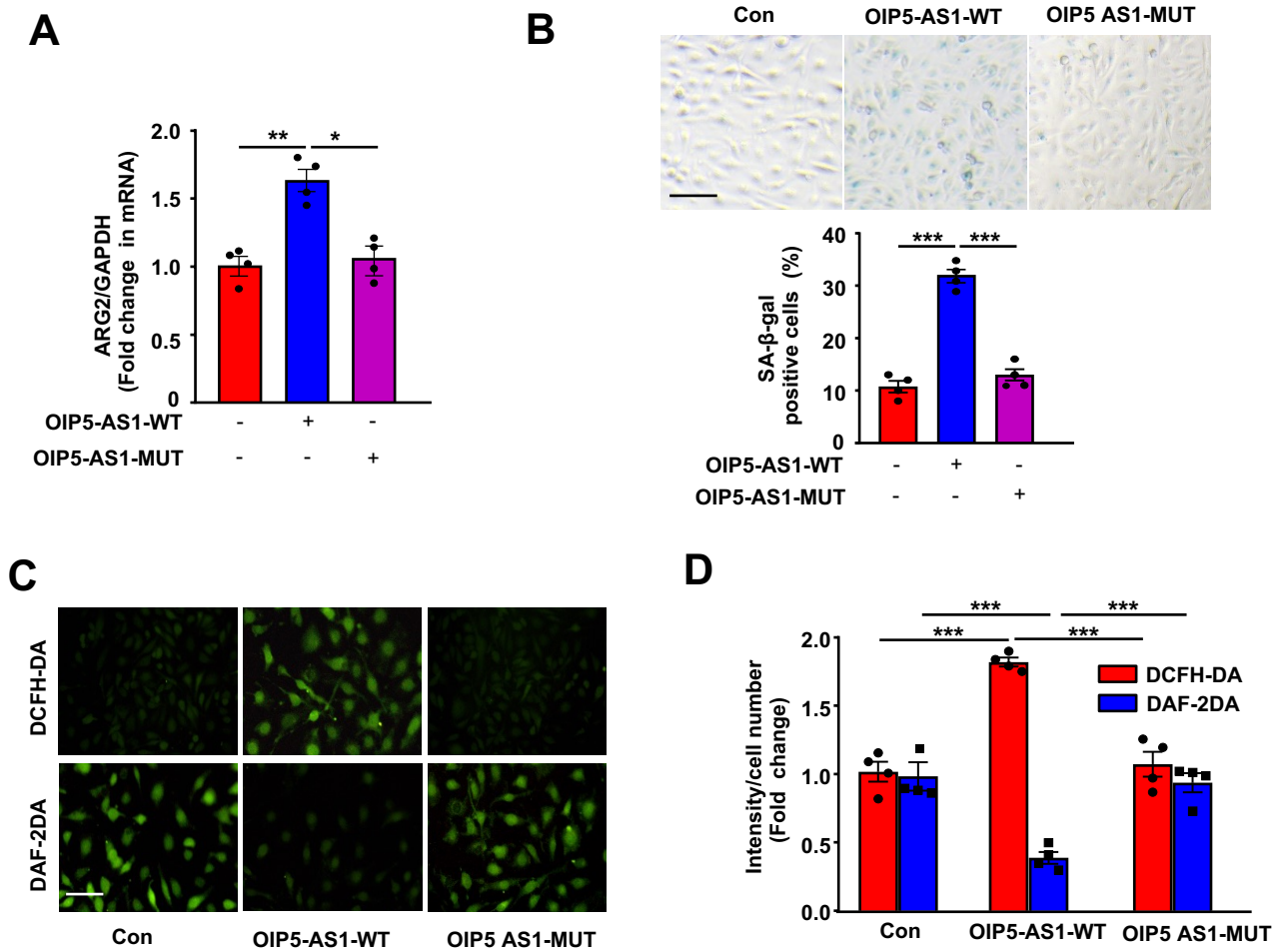
Supplementary Figure 1. miR-4500 mediates H₂O₂-induced endothelial cell aging and dysfunction by targeting ARG2. HUVECs were treated with 100 H₂O₂ for 24 h, then transduced with miR4500 mimics or miR-4500-MUT mimics harboring mutated ARG2-binding sites for 24 h, the cells were subjected to (A) qPCR analysis of ARG2 mRNA expression. (B) SA-β-gal staining for detecting senescent cells. Quantification is presented below the images. (C) DCFH-DA and DAF-2DA staining for the detection of ROS and NO. (D) Quantification of the ROS and NO signals in (C). Scale bar=100 μm. n=4, **p<0.01, ***p<0.001. n.s.: not significant.



Supplementary Figure 2. The lncRNA OIP5-AS1/miR-4500 axis targeting ARG2 modulates H₂O₂-induced premature cellular senescence and endothelial dysfunction HAECs. HAECs were treated with 100 H₂O₂ for 24 h, then transduced with miR4500 mimics or OIP5-AS1 shRNA for 24 h. The cells were subjected to (A) qPCR analysis of ARG2 mRNA expression. (B) SA-β-gal staining for detecting senescent cells. Quantification is presented on the right panel. (C) DCFH-DA and DAF-2DA staining for the detection of ROS and NO. Quantification is presented on the right panel. Scale bar=100 μm. n=4, **p<0.01, ***p<0.001.



Supplementary Figure 3. The expression levels of miR-4500 and OIP5-AS1 in blood serum samples from young and elder people. The qPCR analysis of (A) miR-4500 expression, and (B) OIP5-AS1 expression in the blood samples of young and old people with atherosclerosis. ARG2 mRNA was not detectable in the serum from either group. n=8, **p<0.01, ***p<0.001.



Supplementary Figure 4. OIP5-AS1 promotes endothelial cell senescence via sponging miR-4500. HUVECs were transfected with OIP5-AS1-WT or OIP5-AS1-MUT harboring mutated miR-4500-binding sites. The cells were subjected to (A) qPCR analysis of ARG2 mRNA expression. (B) SA-β-gal staining for detecting senescent cells. Quantification is presented below the images. (C) DCFH-DA and DAF-2DA staining for the detection of ROS and NO. (D) Quantification of the ROS and NO signals in (C). Scale bar=100 μm. n=4, *p<0.05, **p<0.01, ***p<0.001.