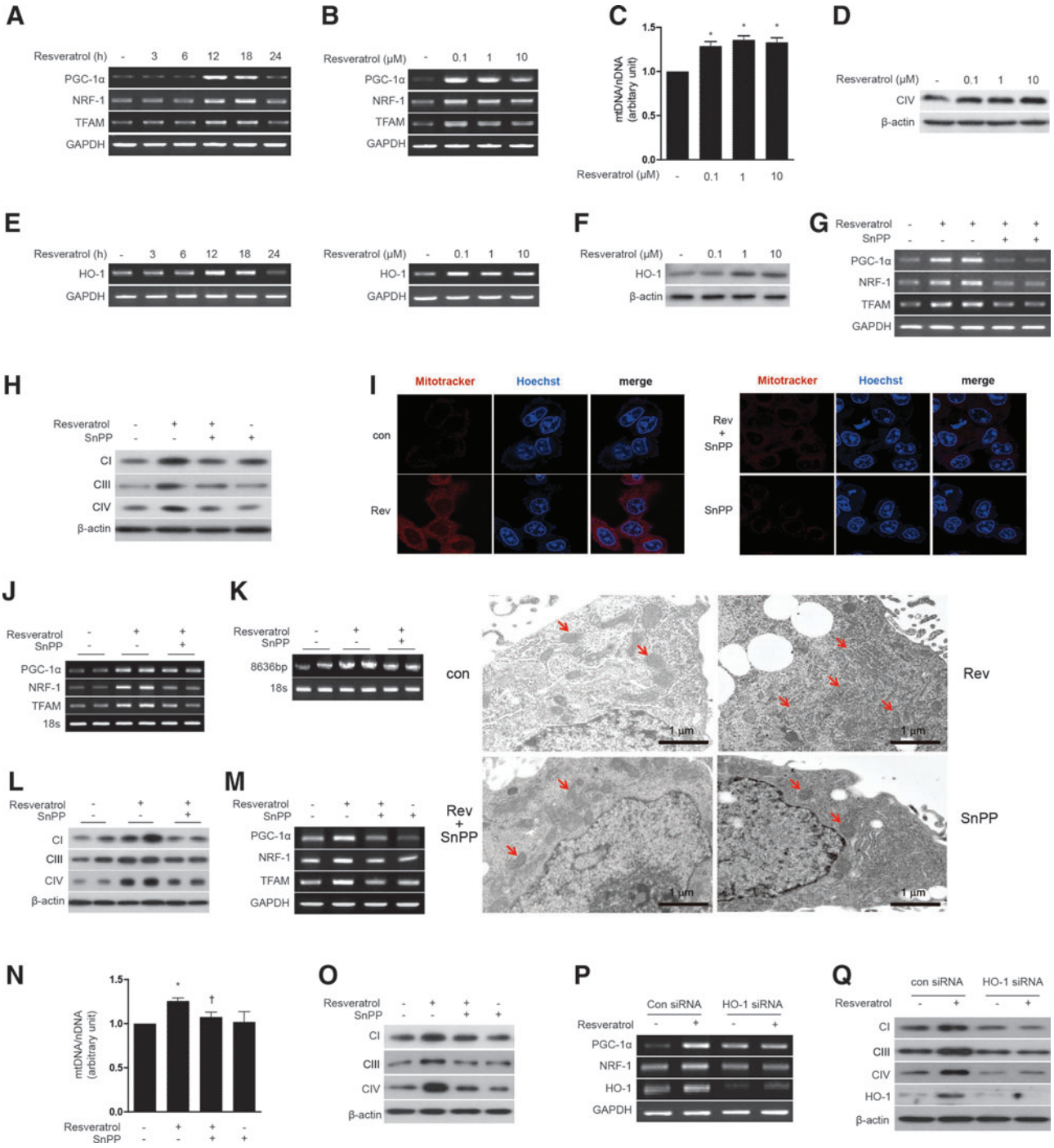

SUPPLEMENTARY FIG. S3. Resveratrol induces mitochondrial biogenesis through the sequential production of NO and CO. (A–F) HepG2 cells were treated with 1 μM of resveratrol for the indicated time intervals and with the indicated concentrations of resveratrol for 12 h. **(G–I)** HepG2 cells were treated with 1 μM resveratrol for 12 h after pretreatment in the absence or presence of 20 μM of SnPP. **(J–L)** C57BL/6 mice, resveratrol (20 mg/kg/day) was given once daily for 7 days by i.p. injection, with or without SnPP pretreatment as indicated. Liver tissues were excised and analyzed for mitochondrial biogenesis in mice. **(M–O)** AML12 cells were treated with 1 μM resveratrol for 12 h after pretreatment in the absence or presence of 20 μM of SnPP. **(P–Q)** HepG2 cells were transfected with control siRNA (con) or HO-1 siRNA that knockdown HO-1 levels. Cells were treated with 1 μM of resveratrol for 12 h. **(A, B, G, J, M, P)** PGC-1α, NRF-1 and TFAM mRNA levels. **(C, K, N)** mtDNA content. **(D, H, L, O, P)** CI (complex I), CIII (complex III), and CIV (complex IV) protein levels. **(E)** HO-1 mRNA levels. **(F)** HO-1 protein levels. **(I)** Mitochondrial mass was assessed by using MitoTracker Red CMXRos staining (red). Nuclei were stained with Hoechst dye (blue). Images of fluorescence were analyzed by confocal microscopy. Mitochondrial biogenesis and morphology was shown by electron microscopy study (red arrows). Scale bar, 1 μm. Experiments were performed thrice independently, and representative data are shown. Data are expressed as mean ± SEM. $^{*}p < 0.05$ compared to control group; $^{\dagger}p < 0.05$ compared to resveratrol group. CO, carbon monoxide; siRNA, small interference RNA; i.p., intraperitoneally.