



**Figure S1.** Detection of ER stress markers in PSC subjected to normoxia or to hypoxia. Cells were incubated in normoxic conditions or under hypoxia and then the cell lysates were processed for Western blotting analysis with specific antibodies. (A) Representative blots showing the detection of the ER chaperone protein BiP/GRP78, the phosphorylation status of eIF2 $\alpha$  and the level of ATF-4. The band corresponding to each protein is marked by an arrow. The molecular weight of each specific protein is given on the right side of each blot. To ensure equal loading of proteins, the levels of  $\beta$ -actin were employed as controls under the tested conditions for BIP and ATF-4, whereas the total expression level of eIF2 $\alpha$  was used as control for p-eIF2 $\alpha$ . (B,C, D) The bars show the quantification of protein levels for BIP ( $58,49 \pm 9,39$ ), p-eIF2 $\alpha$  ( $52,26 \pm 7,54$ ) and ATF-4 ( $63,13 \pm 13,90$ ), which are shown as the mean  $\pm$  SEM of normalized values expressed as % vs cells incubated under normoxia (which was considered 100%). In the graphs, a horizontal dashed line represents the value achieved in cells incubated in normoxia. Data are representative of four independent experiments (HPX, hypoxia; NMX, normoxia; \*,  $P < 0.05$ ; and \*\*\*,  $P < 0.001$  vs normoxia).