Supplementary Figure Legends

Supplementary Fig. 1 Time course of hypoxia-induced apoptosis in Min6 cells. Min6 cells were cultured in normoxia or exposed to hypoxia (1% O_2) for the indicated time points. Apoptosis was assessed by flow cytometry-based TUNEL assay.

Supplementary Fig. 2 mRNA levels of caspase-3, UPR components and Bcl-2 family of proteins at latter time points of hypoxia exposure. Min6 cells were cultured at normoxia or hypoxia at indicated time points. mRNA expression levels were measured by qRTPCR and normalized to β-actin (n=4; values are mean±S.D.).

Supplementary Fig. 3 Analysis of Min6 cells stably expressing a negative control shRNA (Control) or shRNAs targeting HIF-1α (HIF-1α#1, and HIF-1α#2). (**a**) HIF-1α mRNA levels in HIF-1α#1 and HIF-1α#2 cells. (**b**) Hypoxia-dependent induction of BNIP3 is impaired in HIF-1α#1 and HIF-1α#2 cells. Stable cells were exposed to hypoxia (1% O_2) for 24 h or kept at normoxia. Expression levels of HIF-1α and BNIP3 mRNAs were measured by qRTPCR and normalized to β-actin (n=3; values are mean±S.D.; ***P< 0.005 relative to control by two-tailed Student's t test).

Supplementary Fig. 4 Time course of phosphorylated Bad and Bim proteins in response to hypoxia treatment. Min6 cells were exposed to hypoxia for the indicated time points. Cells were treated during 8h with 1 μM thapsigargin (Tg), or 1 μM staurosporine (St). Whole cell extracts were prepared, and proteins were separated by SDS-PAGE and analyzed by immunoblotting with anti-phosphorylated Bad (p-Bad S112), anti-Bim, and anti-β-actin.

Supplementary Fig. 5 Caspase-12 activity is not induced by hypoxia in Min6 cells. Min6 cells were exposed to hypoxia (1% O_2) for the indicated time points or kept at normoxia. Cells were treated with 1 μM thapsigargin (Tg) for 48 h, or 1 μM staurosoporine (St) for 8 h. Caspase-12 activity was measured by a fluorometric assay kit (BioVision) according to manufacturer's instructions (n=4; values are mean±S.D.; ***P< 0.005 relative to control by two-tailed

Student's t test). Results were analyzed using a fluorescence plate reader (Ex/Em = 400/505 nm).

Supplementary Fig. 6 Knockdown efficiency of siRNAs against HIF-1α (**a**), Arnt (**b**), ATF4 (**c**), XBP-1 (**d**), ATF6 (**e**). Min6 cells were transiently transfected with a control siRNA or specific siRNAs against HIF-1α, Arnt, ATF4, XBP-1 and ATF6. 48 h after transfection, cells were exposed to hypoxia for 24 h or kept at normoxia. **f**, **g** UPR transcription factors have no effect on the hypoxia-dependent induction of HIF-1α target genes GLUT1 (**f**) and PGK1 (**g**). Expression levels of HIF-1α, Arnt, ATF4, XBP-1, ATF6, GLUT1 and PGK1 mRNAs were measured by qRTPCR and normalized to β-actin mRNA levels (n=5; values are mean±S.D.; **P < 0.05; ***P< 0.005 relative to control by two-tailed Student's t test).

Supplementary Fig. 7 LC3B-II protein is induced by hypoxia in Min6 cells. (**a**) Hypoxia up-regulates LC3B. Whole cell extract proteins were separated by SDS-PAGE and analyzed by immunoblot assay with anti-LC3B and anti-β-actin antibodies. (**b**) LC3B-II is up-regulated in cells treated with 1 μM of rapamycin.