**Supplementary data**

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Description automatically generatedFigure S1. The ER stressors tunicamycin, brefeldin A or thapsigargin abolish the hypoxia-mediated increase in HIF-1α levels, but does not affect p53 or c-Myc levels**

**(A,C**) HepG2 cells were cultured under normoxia (16% O2) for 24 h, then treated with the ER stressors tunicamycin (Tu, 10 µg/ml), brefeldin A (Br.A, 10 µg/ml) or thapsigargin (Th, 2 µM) and further cultured either under normoxia or hypoxia (5% O2) for 4 h and 24 h. HIF-1, p53 and c-Myc protein levels measured by Western blot under normoxia (16% O2) were set to 1. \*significance 16% O2 vs 5% O2; \*\*significance 16% O2 vs 16% O2 + Tu, Br.A, Th, # significance 5% O2 vs 5% O2 + Tu, Br.A, Th, p ≤ 0.05, n=3. **(B,D)** Representative Western blots of total protein with antibodies against HIF-1, p53, c-Myc, β-actin and -tubulin.

**Graphical user interface

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**(A)** HepG2 cells were transfected with pGL3-HRE-Luc, pGL3-hPAI-796 or pERSE-Luc expression vectors. After transfection, cells were cultured with fresh medium for the next 16 h under normoxia (16% O2), then stimulated with Tu (10 µg/ml) and further cultured either under normoxia or hypoxia (5% O2) for 8 h. In each experiment the percentage of Luc activity was determined relative to the 16% O2 control which was set to 1. \*significance 16% O2 + Tu vs 5% O2 + Tu, \*\*significance 16% O2 vs 16% O2 + Tu, #significance 5% O2 vs 5% O2 + Tu, p ≤ 0.05, n=5. **(B)** HEK 293 cells were cultured under normoxia (16% O2) for 24 h, then treated with Tu (10 µg/ml) and further cultured either under normoxia or hypoxia (5% O2 or 3% O2) for 2 h and 4 h. Total RNA was extracted, and XBP1 mRNA was detected by RT-PCR. XBP1u was observed as a 442-bp band, and XBP1s was observed as a 416-bp band. β-actin served as a loading control. n=3

**Text

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**(A)** HepG2 cells were stimulated with Tu (10 µg/ml) and further cultured for 4 h under normoxic (16% O2) or hypoxic (5% O2) conditions. The pGSK3β (S9), pGSK3α/β (Tyr279/Tyr216), GSK3β and α-tubulin protein levels were measured by Western blot analysis. In each experiment the protein levels in control cells under 16% O2 were set to 1. \*significance 16% O2 + Tu vs 5% O2 + Tu, \*\*significance 16% O2 vs 16% O2 + Tu, #significance 5% O2 vs 5% O2 + Tu, p ≤ 0.05, n=3. **(B)** Representative Western blot analysis with antibodies against pGSK3β (S9), pGSK3α/β (Tyr279/Tyr216), GSK3β and α-tubulin.

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**(A)** HEK 293 cells were transfected with an IPTG-inducible TrCP shRNA expression vector for 48 h and selected with puromycin (2 µg/ml). After selection, cells were subjected to serial dilution and two different clones were stimulated with IPTG-containing media for 72 h and further cultured under normoxia or hypoxia (5% O2) for 4 h. The HIF-1, HIF-2 and -tubulin levels were measured by Western blot analysis. In each experiment the protein levels in control cells under 16% O2 were set to 1. \*significance 16% O2 + Tu vs 5% O2 + Tu, \*\*significance 16% O2 vs 16% O2 + Tu, #significance 5% O2 vs 5% O2 + Tu, p ≤ 0.05, n=3. **(B)** Representative Western blot analysis with antibodies against HIF-1, HIF-2 and α-tubulin.

A picture containing graphical user interface

Description automatically generated**Figure S5. Tunicamycin does not affect LC-3B protein levels**

**(A)** HepG2 cells were stimulated with Tu (10 µg/ml) and further cultured for 4 h under normoxic (16% O2) or hypoxic (5% O2) conditions. The LC-3B and α-tubulin protein levels were measured by Western blot analysis. In each experiment the protein levels in control cells under 16% O2 were set to 1. \*significance 16% O2 + Tu vs 5% O2 + Tu, \*\*significance 16% O2 vs 16% O2 + Tu, #significance 5% O2 vs 5% O2 + Tu, p ≤ 0.05, n=3. **(B)** Representative Western blot analysis with antibodies against LC-3B and α-tubulin.

**Graphical user interface

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**(A)** Real-time proliferation rate of *GSK3* -/- MEFs upon Tu, YC-1 or PT-2385 treatment, \*significance *GSK3* -/- vs *GSK3* -/- + YC-1,\*\*significance *GSK3* -/-*-* vs *GSK3* -/- + PT-2385 p ≤ 0.05, n=4. **(B,C)** Real-time wound closure of *GSK3* -/- cells upon Tu, YC-1 or PT-2385 treatment, \*significance *GSK3* -/- vs Tu, \*\*significance *GSK3* -/- vs YC-1 or PT-2385, p ≤ 0.05, n=3. **(D)** Representative images of wound closure.