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Supplementary data

Supplementary figure 1:

HJV-Hep3B cells were treated according to the described schedule either in normoxia or hypoxia (**Supp 1A**). Cycloheximide was added to inhibit *de novo* protein synthesis and levels of the short-lived protein p27 were measured to confirm the efficacy of the cycloheximide treatment. Immunoblot analysis of total HJV and p27 protein levels are shown for the indicated timepoints in normoxia **(Supp 1B**) and hypoxia (**Supp 1C**). β-Actin levels were measured to correct for loading differences. Signal intensities for HJV and p27 were quantified by densitometer, normalized to β-Actin, and then plotted for the indicated timepoints **(Supp1D & 1E)**. Using the exponential decay function in Excel, HJV protein half life was calculated at ~5.8h both in normoxia and in hypoxia

Supplementary figure 2:

Genomic sequence of human hepcidin promoter showing 140-bp region upstream of TSS with BRE and STAT3 sites indicated. Side-directed mutagenesis of BRE and STAT3 sites is shown **(Supp2A)**. WT-Hep3B cells were transfected with one of the luciferase vectors (wtBRE, mutBRE) in combination with control siRNA or HJV siRNA. Levels of luciferase signal were then measured after 48 hours **(Supp1B)** (*$p<0.001$ using Bonferroni's post-test analysis of one-way ANOVA). WT-Hep3B cells were transfected with one of the luciferase vectors wtBRE **(Supp2C)**, mutBRE **(Supp2D)** or CA9-HRE **(Supp2E)** in combination with control siRNA, TMPRSS6 siRNA or combined HIF-1 & -2α siRNA. Levels of the luciferase signal were then measured after 48h of normoxia or hypoxia (0.5% O_2) (*$p<0.001$ using Bonferroni's post-test analysis of one-way ANOVA). Luciferase signal was normalized to β-galactosidase signal to correct for transfection efficiency.

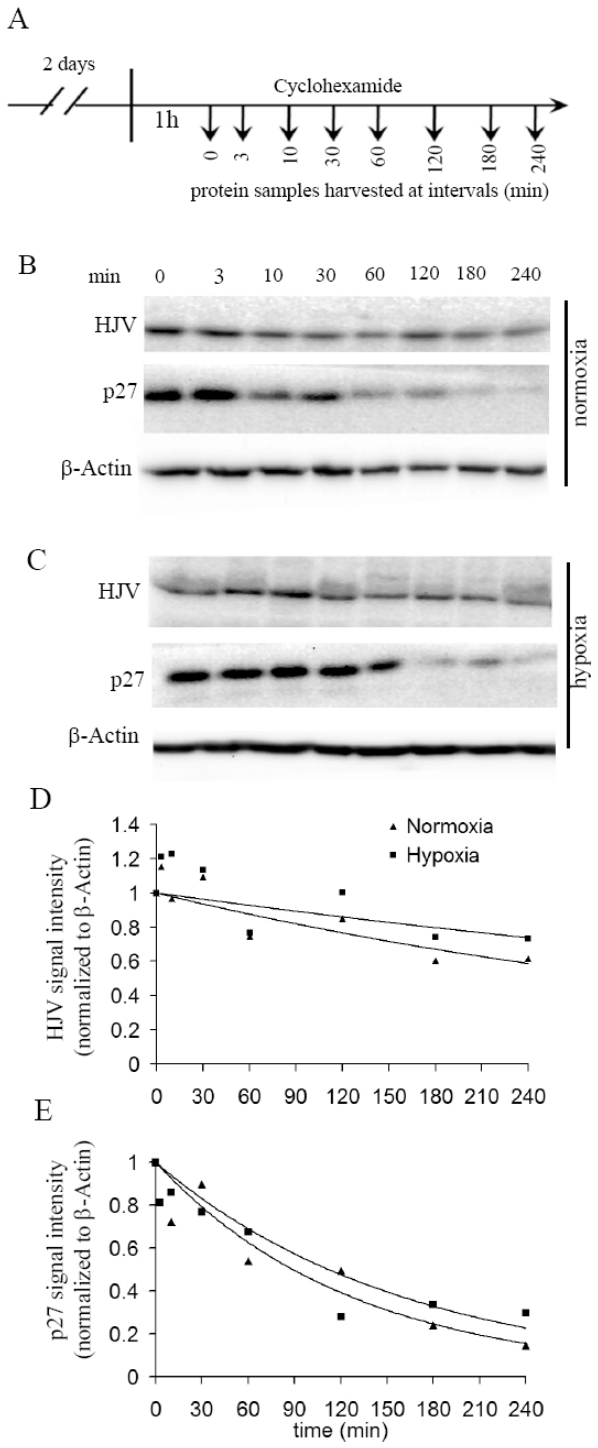
Supplementary figure 3:

HJV-Hep3B cells were transfected with one of the luciferase vectors wtBRE **(Supp3A)**, hepc.prom-2.4kb **(Supp 3B)** or CA9-HRE **(Supp 3C)** in combination with control siRNA, TMPRSS6 siRNA or combined HIF-1 & -2α siRNA. Luciferase activity was then measured after 48h of normoxia or hypoxia (0.5% O_2) (*$p<0.001$ using Bonferroni's post-test analysis of one-way ANOVA). Luciferase signal was normalized to β-galactosidase signal to correct for transfection efficiency.

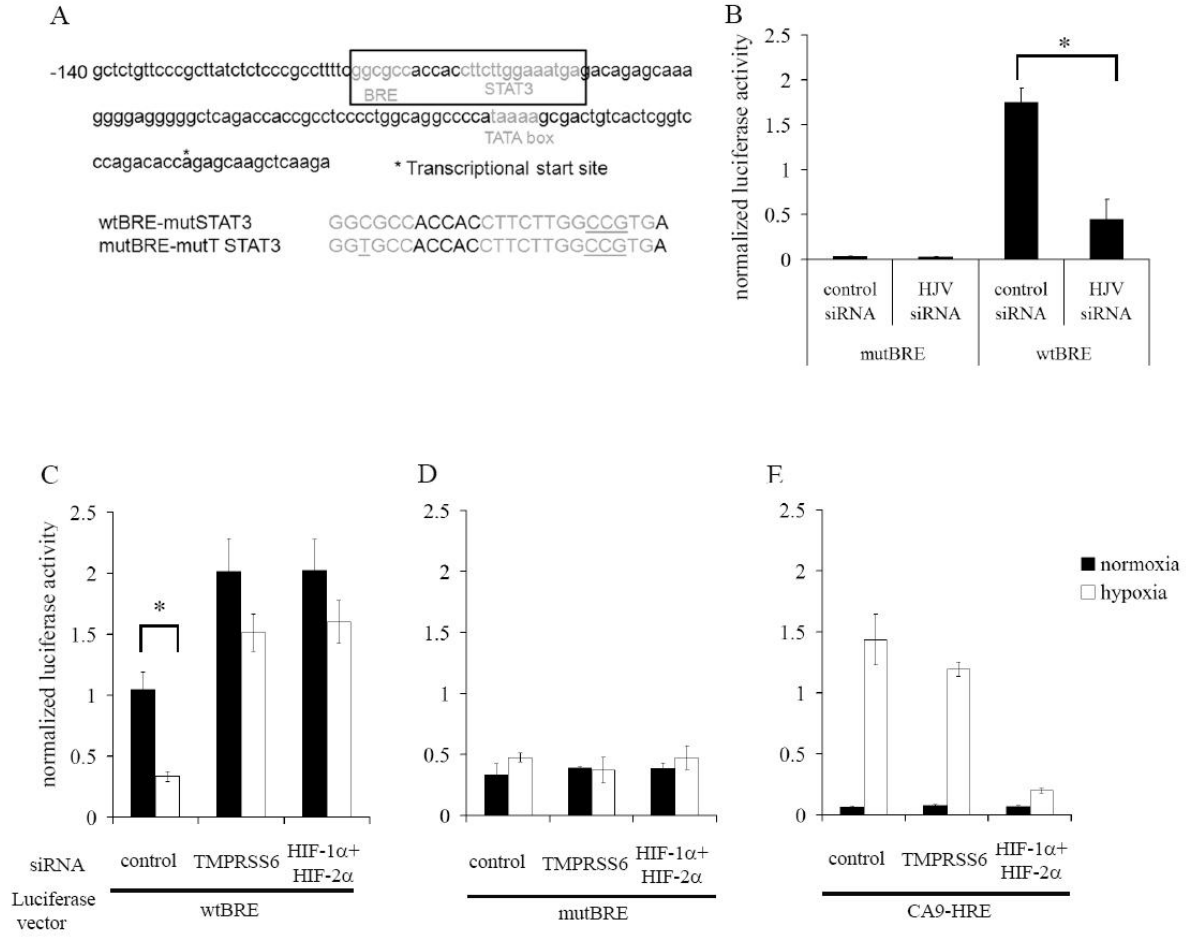
Supplementary figure 4:

Histogram analysis of mHJV **(Supp 4A)** and GFP **(Supp 4B)** expression in HJV-Hep3B pre-transfected with control siRNA, or furin siRNA prior to hypoxia. HJV-Hep3B cells were transfected with the luciferase vector wtBRE **(supp 4C)** or mutBRE **(supp 4D)** in combination with control siRNA, TMPRSS6 siRNA, Furin siRNA or combined TMPRSS6 and Furin siRNA. Levels of the luciferase signal were then measured after 48h of normoxia or hypoxia (0.5% O_2). Luciferase signal was normalized to β-galactosidase signal to correct for transfection efficiency. (*$p<0.001$ using Bonferroni's post-test analysis of one-way ANOVA).

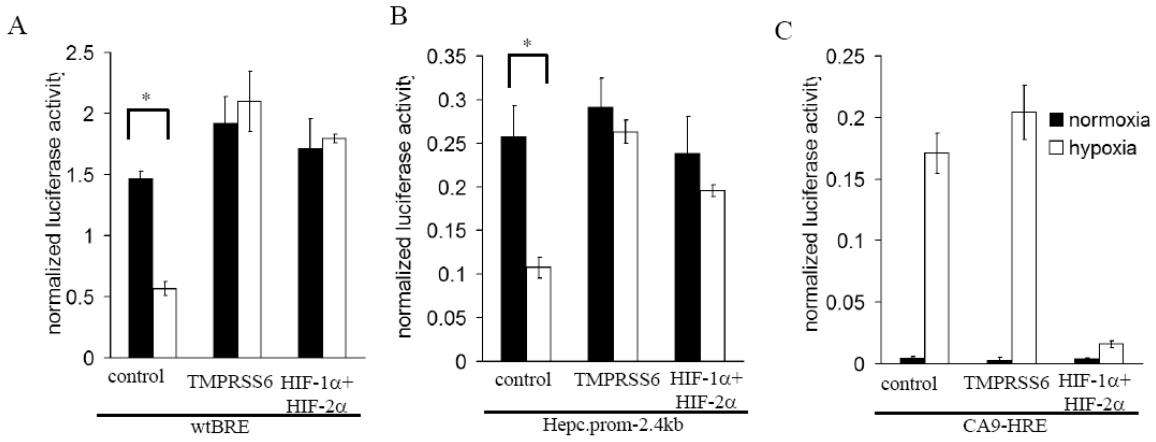
Supplementary figure 1:



Supplementary figure 2:



Supplementary figure 3:



Supplementary figure 4: