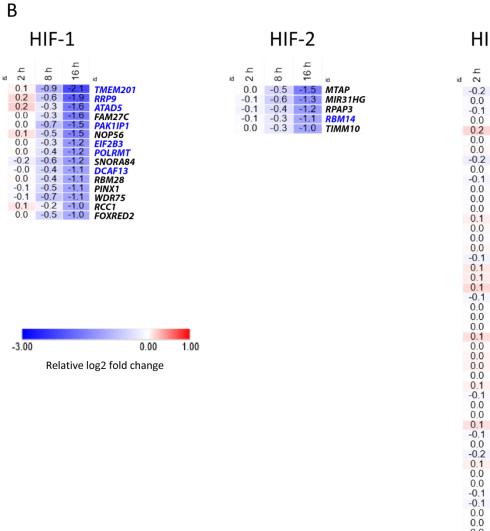


| id | 2 h | 8 h | 16 h | id a | ч | ۲ | 16 h | |
|----|------|-----|------|--------------------|------|-----|------------|--------------------|
| N | 1.4 | 5.3 | 0.1 | id id PTGIS | 2 | ø | - | id |
| | 0.8 | 4.5 | 5.9 | EGLN3 | 0.2 | 1.4 | 1.6 | NARF |
| ł | 2.8 | 5.3 | 5.5 | MIR210HG | 0.1 | 0.5 | 1.6 | PDCD4-AS1 ARVCF |
| | 1.8 | 4.9 | 4.6 | ANGPTL4 | -0.1 | 0.5 | 1.6 1.6 | CFAP57 |
| | 1.9 | 4.0 | 4.1 | ANGPTL4 ANKRD37 | 0.0 | 0.2 | 1.0 | LINC00963 |
| | 0.2 | 2.0 | 3.9 | ADSSL1 | -0.1 | 0.4 | 1.6 | YPEL5 |
| | 0.3 | 2.1 | 3.7 | FAM189A2 | 0.2 | 1.4 | 1.6 | BNIP3 |
| | 0.0 | 2.3 | 37 | ADORA2A | 0.1 | 0.8 | 1.6 | AFAP1L1 |
| | 0.6 | 2.7 | 3.7 | Clorf21 | 0.0 | 1.2 | 1.6 | LINC01116 |
| | 0.1 | 2.2 | 3.4 | SPAG4 | 0.0 | 1.0 | 1.5 | MYCT1 |
| 1 | 0.9 | 2.1 | 3.1 | ARRDC3 | 0.2 | 0.8 | 1.5 | KLF3 |
| | 0.1 | 1.6 | 3.0 | NDRG1 | 0.1 | 1.0 | 1.5 | SLC26A37 |
| | 0.3 | 1.6 | 3.0 | MEGF6 | 0.0 | 0.7 | 1.5 | SLC6A5 |
| | 0.3 | 1.7 | 2.8 | KANK3 | 0.0 | 0.9 | 1.5 | FAM117B |
| | 0.4 | 2.5 | 2.8 | SLC2A1 | 0.0 | 0.6 | 1.5 | ANO6 |
| | -0.1 | 2.0 | 2.7 | MXI1 | 0.0 | 0.1 | 1.5 | BEX2 |
| | 0.1 | 2.3 | 2.7 | VLDLR | 0.0 | 0.5 | 1.5 | PAM |
| | 0.4 | 1.6 | 2.7 | CNKSR3 | 0.1 | 0.9 | 1.5 | PPP1R3B |
| | 0.1 | 1.4 | 2.6 | CXCR4 | 0.2 | 0.2 | 1.5 | SEPT8 |
| | 0.2 | 1.5 | 2.5 | ALDOC | 0.0 | 0.3 | 1.4 | MYO1C |
| | 0.3 | 2.4 | 2.4 | ENO2 | 0.5 | 0.9 | 1.4 | DOK3 |
| | 0.1 | 1.2 | 2.4 | THEM45A | -0.1 | 0.8 | 1.4 | P4HA2 |
| | 0.3 | 1.3 | 2.4 | NFATC4 | -0.2 | 0.2 | 1.4 | GPRC5B |
| | 0.1 | 1.6 | 2.3 | BNIP3L | 0.2 | 0.6 | 1.4 | MEF2D |
| | -0.1 | 0.8 | 2.3 | RGCC | 0.0 | 0.5 | 1.4 | ALPK3 |
| | -0.1 | 0.8 | 2.3 | CSGALNACT1 | 0.0 | 0.5 | 1.4 | YPEL2 F11R |
| | 0.1 | 1.3 | 2.3 | AKAP12 | 0.0 | 0.2 | 1.4 1.4 | FTTR FAM117A |
| | 0.1 | 0.8 | 2.2 | CD109 | 0.0 | 0.4 | 1.4 | EPOR |
| 1 | 1.4 | 1.6 | 2.2 | FLNA | 0.0 | 1.0 | 1.3 | BLCAP |
| 1 | 0.3 | 1.4 | 2.1 | VEGFC | 0.1 | 0.8 | 1.3 | ZNF436 |
| | 0.1 | 1.3 | 2.1 | P4HA1 | 0.1 | 0.5 | 1.3 | IER3 |
| | 0.0 | 0.7 | 2.0 | MTSS1 | 0.1 | 0.5 | 1.3 | OTUD1 |
| | 0.1 | 1.0 | 2.0 | MAGI1 | 0.1 | 0.3 | 1.3 | CTNNBIP1 |
| | 0.1 | 1.3 | 2.0 | PGM1 | 0.0 | 0.8 | 1.3 | TMCC1 |
| | 0.3 | 1.2 | 1.9 | PTPRB | 0.1 | 0.4 | 1.2 | ZNF532 |
| | 0.4 | 1.4 | 1.9 | INHBA | 0.3 | 1.5 | 1.2 | ANKZF1 |
| | 0.3 | 1.1 | 1.9 | ZNF436-AS1 | -0.2 | 0.3 | 1.2 | RPS29 |
| | -0.1 | 0.9 | 1.9 | C20orf195 | 0.4 | 1.2 | 1.2 | PDK1 |
| | 0.0 | 0.3 | 1.9 | SNCAIP | 0.2 | 0.6 | 1.2 | RAD51-AS1 |
| | -0.2 | 0.6 | 1.9 | CHADL | 0.1 | 0.4 | 1.2 | NPEPL1 |
| | 0.2 | 0.8 | 1.8 | TNFRSF14 | 0.0 | 0.7 | 1.2 | UGCG |
| | 0.4 | 1.2 | 1.8 | MAP3K8 | 0.0 | 0.8 | 1.2 | CHSY1 |
| | -0.1 | 0.7 | 1.8 | RASSF2 | 0.1 | 0.3 | 1.2 | COL4A2 |
| | 0.1 | 0.7 | 1.8 | TCF7L1 | 0.0 | 0.5 | 1.1 | MYO1E |
| | 0.0 | 0.5 | 1.8 | HSBP1L1 | 0.0 | 0.3 | 1.1 | LGALS3 |
| | 0.2 | 1.4 | 1.8 | APOLD1 | -0.2 | 0.8 | 1.1 | CBX2 BCL6B |
| | 0.3 | 1.2 | 1.8 | SLC25A37 | -0.2 | 0.1 | 1.1 | DDAH2 |
| | 0.1 | 1.3 | 1.7 | PPP1R13L | 0.0 | 0.4 | 1.1 | ERO1L |
| | 0.0 | 0.9 | 1.7 | TMEM44 | 0.0 | 0.3 | 1.1 | Clorf198 |
| | 0.1 | 1.3 | 1.7 | C8orf58 | 0.1 | 0.5 | 1.1 | SGK223 |
| | 0.0 | 2.6 | 1.7 | PFKFB4 | 0.0 | 0.5 | 1.0 | PHF10 |
| | 0.2 | 0.4 | 1.7 | UBA7 | | | | |

HIF-1/HIF-2

Supplemental Figure 3. *Hypoxia induced changes in expression of HRE motifs containing genes significantly affected during hypoxia.* Heat maps representing the significant (P < 0.005) expression changes of unique HIF-1, HIF-2, and HIF-1/HIF-2 upregulated (*A*) and reduced (*B*) transcripts during 2h, 8h and 16h of hypoxia are provided in (A). The *HRE* motifs containing genes in agreement with Smythies JA et al. 2019(43) are depicted with red (for upregulated set A) and blue (for downregulated set B) and combined in **Supplemental Table 1C**. Heat maps were generated with Morpheus software (Morpheus, https://software.broadinstitute.org/morpheus).



HIF-1/HIF-2

| id | 2 h | 8 h | 16 h | id |
|----|------|------|------|------------|
| | -0.2 | -1.8 | -2.3 | SPSB2 |
| | 0.0 | -1.0 | -2.2 | VPS9D1-AS1 |
| | -0.1 | -0.8 | -1.9 | PPAT |
| | 0.0 | -0.5 | -1.8 | DHODH |
| | 0.2 | | | |
| | | -0.1 | | CAPN15 |
| | 0.0 | -0.7 | -1.8 | SNORA24 |
| | 0.0 | -0.6 | -1.7 | PDSS1 |
| | -0.2 | -0.6 | -1.6 | ABCE1 |
| | 0.0 | -0.8 | -1.6 | GE MIN5 |
| | -0.1 | -0.8 | -1.6 | AMD1 |
| | 0.0 | -0.6 | -1.6 | GRWD1 |
| | 0.0 | -0.4 | -1.6 | SGMS2 |
| | 0.0 | -0.4 | -1.6 | HGH1 |
| | | | -1.6 | |
| | 0.1 | -0.2 | -1.0 | BOP1 |
| | 0.0 | -0.6 | -1.5 | PYCRL |
| | 0.0 | -0.2 | -1.5 | ТМЕМ38В |
| | 0.0 | -0.7 | -1.5 | EEF2KMT |
| | -0.1 | -0.8 | -1.5 | ZNF593 |
| | 0.1 | -0.3 | -1.4 | XRCC2 |
| | 0.1 | -0.6 | -1.4 | SNHG17 |
| | 0.1 | -0.3 | -1.4 | POLR1A |
| | -0.1 | -0.5 | -1.4 | |
| | | | -1.4 | EFHD2 |
| | 0.0 | -0.6 | -1.3 | NOP58 |
| | 0.0 | -0.5 | -1.3 | NAA50 |
| | 0.0 | -0.2 | -1.3 | ATIC |
| | 0.1 | -0.2 | -1.3 | MDN1 |
| | 0.0 | -0.3 | -1.3 | NRG1 |
| | 0.0 | -0.3 | -1.3 | IMP4 |
| | 0.0 | -0.4 | -1.3 | SLC19A1 |
| | 0.0 | -0.4 | -1.3 | POLR2D |
| | 0.1 | -0.7 | -1.2 | ZNRF3 |
| | -0.1 | -0.5 | -1.2 | |
| | | | -1.2 | EIF4E |
| | 0.0 | -0.6 | -1.2 | RSAD1 |
| | 0.0 | -0.3 | -1.2 | PRR7 |
| | 0.1 | 0.0 | -1.2 | NR2F1 |
| | -0.1 | -0.7 | -1.2 | EXOSC4 |
| | 0.0 | -0.4 | -1.1 | YDJC |
| | -0.2 | -0.3 | -1.1 | EIF5B |
| | 0.1 | -0.5 | -1.1 | KRI1 |
| | 0.0 | -0.5 | -1.1 | RPUSD1 |
| | 0.0 | -0.3 | -1.1 | MRPL12 |
| | -0.1 | -0.2 | -1.1 | TCOF1 |
| | -0.1 | -0.2 | -1.1 | FKBP4 |
| | 0.0 | -0.2 | -1.1 | |
| | | | -1.1 | NLE1 |
| | 0.0 | -0.4 | -1.1 | SSSCA1 |
| | 0.0 | -0.3 | -1.1 | C1QBP |
| | 0.0 | -0.2 | -1.1 | CSE1L |
| | 0.0 | -0.4 | -1.1 | ATR |
| | 0.0 | -0.2 | -1.0 | NCLN |
| | 0.0 | -0.6 | -1.0 | SLC25A28 |
| | 0.0 | -0.3 | -1.0 | MRPL4 |
| | 0.0 | -0.5 | -1.0 | GEMIN4 |
| | 0.0 | -0.3 | -1.0 | DIS3L |
| | -0.1 | -0.4 | -1.0 | RAD51D |
| | 0.1 | 0.4 | 1.0 | NADSID |

Supplemental Figure 3. Hypoxia induced changes in expression of HRE motifs containing genes significantly affected during hypoxia. Heat maps representing the significant (p-value below P < 0.005) expression changes of unique HIF-1, HIF-2, and HIF-1/HIF-2 upregulated (A) and reduced (B) transcripts during 2h, 8h and 16h of hypoxia are provided in (A). The HRE motifs containing genes in agreement with Smythies JA et al. 2019(43) are depicted with red (for upregulated set A) and blue (for downregulated set B) and combined in Supplemental Table 1C. Heat generated Morpheus software maps were with (Morpheus, https://software.broadinstitute.org/morpheus).