**Supplementary Methods**

**Curation of founder hypoxia gene sets**

From two recent review papers, *i.e.* Yang et al. (2018, PMID: 29513038) 1 and Harris et al. (2015, PMID: 26282471) 2, we curated a number of founder hypoxia gene set. The studies that include only bioinformatics analysis without *in vitro* or *in vivo* experiment were removed as lacking direct evidence of hypoxia relevance. We further excluded any study that derives gene expression signatures using patient prognosis information, as the resultant gene signature could reflect biological parameters beyond hypoxia. With a couple of exceptions detailed below, we removed the publications that only studied one single cell line, as those would have high false positive rates. Elvidge et al. (2006, PMID: 16565084) 3 and Aprelikova et al. (2006, PMID: 16740701) 4 both studied MCF7 breast cancer cell line but under different time points and hypoxia concentrations. Therefore the overlap between the two was used to increase confidence. Wang et al. (2005, PMID: 15833863) 5 studied one cell line but performed extra microarray studies after HIF transfection, and therefore was of high confidence and included in our study. Among the remaining studies, Mense et al. (2006, PMID: 16507782) 6, Bosco (2006, PMID: 16849508) 7 and Detwiller et al. (2005, PMID: 15994966) 8 were removed as the gene sets were re-analysed and represented in Benita et al. (2009, PMID: 19491311) 9. Seigneuric et al. (2007, PMID: 17532074) 10 was removed as data was from and represented by Chi et al. (2006, PMID: 16417408) 11. Jogi et al. (2004, PMID: 15093745) 12 was removed as a similar but more comprehensive study was performed by Fardin (2010, PMID: 20652058) 13, which was included in this study. For Fjeldbo et al. (2016, PMID: 27012812) 14, we used genes inducible by hypoxia in more than 6 cell lines. Most of the above literature included in this study provided genes both induced and suppressed by hypoxia, defined as per original publication. We only kept the genes inducible by hypoxia in each founder gene set. Furthermore, a hallmark hypoxia gene set was collected from Molecular Signatures Database. Another expert curated hypoxia gene set was taken from Harris (2002, PMID: 11902584) 15.

Gene symbols from the old studies could be out-dated. For each founder gene set, we downloaded the gene alias from the original publication and converted them to the latest official gene symbols using alias2Symbol function from LIMMA package and org.Hs.eg.db library as annotation, all available in Bioconductor.

**Supplementary Table S1** 12 founder hypoxia gene sets curated

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Study | PubMed ID | Site | Cell line/Tissue | O2%/ Time | Size | Comment |
| Sorensen (2010) | 20429727 | Head&neck | FaDuDD, UtScc5, UtScc14, UTSCC15 | 5%,1%,0.1%,0.01%,0%/ 24hrs | 27 | Hypoxia inducible in ≥3 cell lines & pH independent |
| Fardin (2010) | 20624283 | Neuroblastoma | GI-LI-N, ACN, SHEP-2, SK-N-BE2(C), IMR-32, SK-N-F1, LAN-1, SK-N-SH, GI-ME-N, SHEP-21N | 1%/ 18hrs | 32 | Inducible by hypoxia in all 11 lines |
| Benita (2009) | 19491311 | Glioblastoma,  Cervix, Breast, Astrocytes, monocytes, B cells | MCF7, U251, Astrocytes, monocytes, B cells, HeLa |  | 60 | Top predicted HIF-target/ Inducible by hypoxia ≥3 cell types |
| Sung (2007) | 17320280 | Nasopharynx | CNE-20, HONE-1 | 0.1%/16hrs | 90 | Inducible by hypoxia in both cell lines |
| Chi (2006) | 16417408 | Epithelial cells | Human mammalian epithelial cells, renal proximal tubule epithelial cells | 2%&0.02%/ 1,3,6,12,24hrs | 119 |  |
| Wang (2005)\* | 15833863 | Embryonic kidney cells | HEK293T | 1%/16hrs | 56 | Inducible by hypoxia or by transfected with HIF 1α, HIF-1α mut, or HIF-2α |
| Elvidge (2006)^  Aprelikova (2006)^ | 16565084  16740701 | Breast | MCF7 | 0.5%/8hrs,  1%/16hrs | 84 | Overlap between two gene lists |
| Fjeldbo (2016) | 27012812 | Cervix | HeLa, SW756, C-33 A, C-4I, ME-180, HT-3, SiHa, CaSki | 0.2%/ 24hrs | 43 | Inducible by hypoxia in ≥6 cell lines |
| Ragnum (2014) | 25461803 | Prostate | 39 primary tumors |  | 32 | Genes correlated with pimonidazole staining |
| Yang (2017) | 29423096 | Sarcoma | 93T449, HT1080, SKUT1, SNF96-2, SW684, SW872, SW982 | 1%/24hrs | 34 | Inducible by hypoxia in all 7 lines |
| Hallmark Hypoxia |  | Breast, non-small cell lung cancer, melanoma, Epithelial Cells |  |  | 200 | Expert curation from Molecular Signatures Database |
| Harris (2002) | 11902584 |  |  |  |  | Expert curation |

\*This single cell line study was included because additional HIF transfection experiment was performed to increase the confidence of finding.

^The two reports studied the same cell line but on different O2 concentration of time points. Therefore the overlap of the two gene lists was used in this work.

**Supplementary Table S2** Details of the 52 core hypoxia genes. Frequency denotes the number of times a gene appears in 12 founder gene sets

|  |  |  |  |
| --- | --- | --- | --- |
| SYMBOL | ENTREZID | GENENAME | Frequency |
| BNIP3L | 665 | BCL2 interacting protein 3 like | 10 |
| FAM162A | 26355 | family with sequence similarity 162 member A | 10 |
| P4HA1 | 5033 | prolyl 4-hydroxylase subunit alpha 1 | 10 |
| BHLHE40 | 8553 | basic helix-loop-helix family member e40 | 9 |
| BNIP3 | 664 | BCL2 interacting protein 3 | 9 |
| NDRG1 | 10397 | N-myc downstream regulated 1 | 9 |
| P4HA2 | 8974 | prolyl 4-hydroxylase subunit alpha 2 | 9 |
| PGK1 | 5230 | phosphoglycerate kinase 1 | 9 |
| ADM | 133 | adrenomedullin | 8 |
| ALDOC | 230 | aldolase, fructose-bisphosphate C | 8 |
| DDIT4 | 54541 | DNA damage inducible transcript 4 | 8 |
| HK2 | 3099 | hexokinase 2 | 8 |
| IGFBP3 | 3486 | insulin like growth factor binding protein 3 | 8 |
| KDM3A | 55818 | lysine demethylase 3A | 8 |
| CCNG2 | 901 | cyclin G2 | 7 |
| ERO1A | 30001 | endoplasmic reticulum oxidoreductase 1 alpha | 7 |
| MXI1 | 4601 | MAX interactor 1, dimerization protein | 7 |
| PDK1 | 5163 | pyruvate dehydrogenase kinase 1 | 7 |
| SLC2A1 | 6513 | solute carrier family 2 member 1 | 7 |
| ANKRD37 | 353322 | ankyrin repeat domain 37 | 6 |
| HILPDA | 29923 | hypoxia inducible lipid droplet associated | 6 |
| INSIG2 | 51141 | insulin induced gene 2 | 6 |
| PFKFB3 | 5209 | 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3 | 6 |
| SLC2A3 | 6515 | solute carrier family 2 member 3 | 6 |
| STC2 | 8614 | stanniocalcin 2 | 6 |
| VEGFA | 7422 | vascular endothelial growth factor A | 6 |
| ZNF395 | 55893 | zinc finger protein 395 | 6 |
| ANGPTL4 | 51129 | angiopoietin like 4 | 5 |
| ENO2 | 2026 | enolase 2 | 5 |
| FOS | 2353 | Fos proto-oncogene, AP-1 transcription factor subunit | 5 |
| GBE1 | 2632 | 1,4-alpha-glucan branching enzyme 1 | 5 |
| LDHA | 3939 | lactate dehydrogenase A | 5 |
| LOX | 4015 | lysyl oxidase | 5 |
| PFKFB4 | 5210 | 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 4 | 5 |
| PPFIA4 | 8497 | PTPRF interacting protein alpha 4 | 5 |
| STC1 | 6781 | stanniocalcin 1 | 5 |
| WSB1 | 26118 | WD repeat and SOCS box containing 1 | 5 |
| AK3 | 50808 | adenylate kinase 3 | 4 |
| AK4 | 205 | adenylate kinase 4 | 4 |
| ALDOA | 226 | aldolase, fructose-bisphosphate A | 4 |
| BTG1 | 694 | BTG anti-proliferation factor 1 | 4 |
| CA9 | 768 | carbonic anhydrase 9 | 4 |
| CXCR4 | 7852 | C-X-C motif chemokine receptor 4 | 4 |
| EFNA3 | 1944 | ephrin A3 | 4 |
| EGLN3 | 112399 | egl-9 family hypoxia inducible factor 3 | 4 |
| GADD45B | 4616 | growth arrest and DNA damage inducible beta | 4 |
| GAPDH | 2597 | glyceraldehyde-3-phosphate dehydrogenase | 4 |
| GPI | 2821 | glucose-6-phosphate isomerase | 4 |
| GYS1 | 2997 | glycogen synthase 1 | 4 |
| PFKP | 5214 | phosphofructokinase, platelet | 4 |
| PLOD2 | 5352 | procollagen-lysine,2-oxoglutarate 5-dioxygenase 2 | 4 |
| ZNF292 | 23036 | zinc finger protein 292 | 4 |

**Supplementary Table S3** Hallmark gene sets associated with hypoxia gene expression phenotypes in pan cancer analysis by GSEA

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| HALLMARK GENE SET | SIZE | ES | NES | NOM p-val | FDR q-val | FWER p-val |
| EPITHELIAL\_MESENCHYMAL\_TRANSITION | 196 | 0.764 | 3.331 | 0 | 0 | 0 |
| TNFA\_SIGNALING\_VIA\_NFKB | 197 | 0.765 | 3.326 | 0 | 0 | 0 |
| HYPOXIA | 194 | 0.756 | 3.290 | 0 | 0 | 0 |
| INFLAMMATORY\_RESPONSE | 196 | 0.659 | 2.905 | 0 | 0 | 0 |
| MTORC1\_SIGNALING | 195 | 0.664 | 2.892 | 0 | 0 | 0 |
| GLYCOLYSIS | 198 | 0.656 | 2.824 | 0 | 0 | 0 |
| G2M\_CHECKPOINT | 194 | 0.632 | 2.776 | 0 | 0 | 0 |
| E2F\_TARGETS | 194 | 0.626 | 2.715 | 0 | 0 | 0 |
| INTERFERON\_GAMMA\_RESPONSE | 197 | 0.626 | 2.714 | 0 | 0 | 0 |
| ANGIOGENESIS | 35 | 0.790 | 2.622 | 0 | 0 | 0 |
| IL6\_JAK\_STAT3\_SIGNALING | 87 | 0.657 | 2.559 | 0 | 0 | 0 |
| MYC\_TARGETS\_V1 | 197 | 0.590 | 2.556 | 0 | 0 | 0 |
| APOPTOSIS | 158 | 0.593 | 2.501 | 0 | 0 | 0 |
| IL2\_STAT5\_SIGNALING | 194 | 0.573 | 2.500 | 0 | 0 | 0 |
| COMPLEMENT | 194 | 0.565 | 2.468 | 0 | 0 | 0 |
| ALLOGRAFT\_REJECTION | 198 | 0.567 | 2.447 | 0 | 0 | 0 |
| P53\_PATHWAY | 194 | 0.563 | 2.447 | 0 | 0 | 0 |
| APICAL\_JUNCTION | 191 | 0.535 | 2.338 | 0 | 0 | 0 |
| INTERFERON\_ALPHA\_RESPONSE | 93 | 0.588 | 2.318 | 0 | 0 | 0 |
| TGF\_BETA\_SIGNALING | 53 | 0.632 | 2.283 | 0 | 0 | 0 |
| COAGULATION | 135 | 0.542 | 2.268 | 0 | 0 | 0 |
| KRAS\_SIGNALING\_UP | 194 | 0.508 | 2.225 | 0 | 0 | 0 |
| UV\_RESPONSE\_UP | 154 | 0.508 | 2.156 | 0 | 0 | 0 |
| MITOTIC\_SPINDLE | 197 | 0.486 | 2.123 | 0 | 0 | 0 |
| UNFOLDED\_PROTEIN\_RESPONSE | 110 | 0.492 | 1.979 | 0 | 4.40E-05 | 0.001 |
| CHOLESTEROL\_HOMEOSTASIS | 72 | 0.514 | 1.944 | 0 | 4.23E-05 | 0.001 |
| UV\_RESPONSE\_DN | 138 | 0.445 | 1.854 | 0 | 2.48E-04 | 0.006 |
| MYC\_TARGETS\_V2 | 58 | 0.507 | 1.825 | 0 | 2.39E-04 | 0.006 |
| MYOGENESIS | 199 | 0.412 | 1.785 | 0 | 4.24E-04 | 0.011 |
| NOTCH\_SIGNALING | 32 | 0.535 | 1.717 | 0.007564 | 8.35E-04 | 0.022 |
| ESTROGEN\_RESPONSE\_LATE | 194 | 0.392 | 1.692 | 0 | 0.001095 | 0.03 |
| ANDROGEN\_RESPONSE | 99 | 0.416 | 1.659 | 0.001321 | 0.001809 | 0.05 |
| PI3K\_AKT\_MTOR\_SIGNALING | 104 | 0.417 | 1.659 | 0 | 0.001754 | 0.05 |
| HEDGEHOG\_SIGNALING | 35 | 0.499 | 1.632 | 0.008785 | 0.002506 | 0.074 |
| REACTIVE\_OXIGEN\_SPECIES\_PATHWAY | 46 | 0.465 | 1.605 | 0.005806 | 0.003394 | 0.103 |
| ESTROGEN\_RESPONSE\_EARLY | 193 | 0.348 | 1.524 | 0.003567 | 0.008507 | 0.237 |
| FATTY\_ACID\_METABOLISM | 157 | -0.339 | -1.674 | 0 | 0.002615 | 0.013 |
| BILE\_ACID\_METABOLISM | 110 | -0.423 | -1.970 | 0 | 0 | 0 |

Size: number of genes in the pathway; ES: gene set enrichment score; NES: normalised enrichment score; NOM p-val: nominal p values; FDR q-val: false discovery rate adjusted nominal p values; FWER p-val: familywise-error rate adjusted nominal p values.

**Supplementary Table S4** Proteins associated with hypoxia gene expression phenotypes in pan-cancer analysis. Positive coefficients indicate induced by hypoxia and negative coefficients indicate hypoxia repression.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| TCGA protein symbol | Coefficient | P-value | 2.5% CI | 97.5% CI | FDR |
| PAI1 | 0.451837731 | 7.20E-117 | 0.414025 | 0.48965 | 1.43E-114 |
| FIBRONECTIN | 0.377122052 | 2.35E-79 | 0.338428 | 0.415816 | 2.33E-77 |
| CASPASE3 | 0.297501163 | 0.002772 | 0.103206 | 0.491797 | 0.004426 |
| GAPDH | 0.296231466 | 1.22E-48 | 0.256918 | 0.335545 | 4.03E-47 |
| NDRG1\_pT346 | 0.272271547 | 2.25E-57 | 0.239146 | 0.305397 | 1.49E-55 |
| ANNEXIN1 | 0.234628172 | 7.98E-32 | 0.195645 | 0.273612 | 1.75E-30 |
| EGFR | 0.214444945 | 9.11E-29 | 0.176839 | 0.25205 | 1.64E-27 |
| TFRC | 0.204476154 | 1.52E-31 | 0.170342 | 0.23861 | 3.00E-30 |
| YB1\_pS102 | 0.202945877 | 1.70E-19 | 0.159024 | 0.246868 | 1.87E-18 |
| X4EBP1 | 0.180021815 | 2.25E-16 | 0.137133 | 0.222911 | 2.03E-15 |
| ASNS | 0.171850986 | 3.13E-15 | 0.129226 | 0.214476 | 2.30E-14 |
| CD49B | 0.164485615 | 3.11E-16 | 0.12511 | 0.203861 | 2.68E-15 |
| X4EBP1\_pT70 | 0.14093957 | 2.85E-10 | 0.097196 | 0.184684 | 1.34E-09 |
| HSP70 | 0.138903413 | 3.53E-10 | 0.095562 | 0.182245 | 1.63E-09 |
| CYCLINB1 | 0.128908612 | 2.42E-14 | 0.095842 | 0.161976 | 1.60E-13 |
| AKT\_pT308 | 0.12528119 | 4.05E-09 | 0.083583 | 0.166979 | 1.67E-08 |
| BID | 0.115013869 | 7.66E-07 | 0.069452 | 0.160576 | 2.41E-06 |
| DVL3 | 0.113464116 | 1.54E-07 | 0.07112 | 0.155808 | 5.01E-07 |
| TAZ | 0.107386592 | 2.43E-06 | 0.062763 | 0.15201 | 7.09E-06 |
| MIG6 | 0.104711985 | 4.75E-08 | 0.067161 | 0.142263 | 1.78E-07 |
| S6\_pS235S236 | 0.104129581 | 9.10E-06 | 0.058163 | 0.150097 | 2.23E-05 |
| X4EBP1\_pS65 | 0.102467094 | 4.68E-06 | 0.058631 | 0.146303 | 1.22E-05 |
| X1433ZETA | 0.101255184 | 1.47E-06 | 0.060072 | 0.142439 | 4.47E-06 |
| MYOSINIIA\_pS1943 | 0.10107472 | 5.08E-08 | 0.064749 | 0.1374 | 1.83E-07 |
| VHL | 0.098165103 | 9.53E-07 | 0.058936 | 0.137394 | 2.95E-06 |
| MEK1\_pS217S221 | 0.096500497 | 2.99E-05 | 0.051215 | 0.141786 | 6.79E-05 |
| G6PD | 0.095645469 | 3.19E-05 | 0.0506 | 0.140691 | 7.17E-05 |
| IGFBP2 | 0.093819009 | 2.95E-06 | 0.054508 | 0.13313 | 8.33E-06 |
| YAP | 0.090367512 | 4.89E-05 | 0.046771 | 0.133964 | 0.000104 |
| P21 | 0.088357626 | 3.81E-05 | 0.046331 | 0.130384 | 8.29E-05 |
| CASPASE7CLEAVEDD198 | 0.087737571 | 4.38E-05 | 0.045677 | 0.129798 | 9.42E-05 |
| AKT\_pS473 | 0.082881025 | 0.000112 | 0.04084 | 0.124922 | 0.000229 |
| EGFR\_pY1068 | 0.078145392 | 0.000188 | 0.037144 | 0.119147 | 0.000373 |
| EEF2 | 0.07703482 | 0.000206 | 0.036369 | 0.117701 | 0.000403 |
| EIF4G | 0.076251731 | 0.000798 | 0.031697 | 0.120807 | 0.001386 |
| YAP\_pS127 | 0.075271906 | 0.0004 | 0.033614 | 0.11693 | 0.000733 |
| BAX | 0.07504428 | 0.000895 | 0.030777 | 0.119312 | 0.00154 |
| EGFR\_pY1173 | 0.07001179 | 0.001116 | 0.027924 | 0.1121 | 0.001888 |
| S6\_pS240S244 | 0.069303136 | 0.002637 | 0.024142 | 0.114464 | 0.00428 |
| VEGFR2 | 0.066325321 | 0.000168 | 0.031789 | 0.100861 | 0.000336 |
| CHK2\_pT68 | 0.06604895 | 0.003213 | 0.022123 | 0.109975 | 0.00509 |
| MEK1 | 0.060318271 | 0.001278 | 0.023621 | 0.097015 | 0.002145 |
| BAK | -0.058588711 | 0.000137 | -0.08869 | -0.02848 | 0.000277 |
| RAB25 | -0.059166177 | 0.001328 | -0.09528 | -0.02305 | 0.002209 |
| CAVEOLIN1 | -0.060414669 | 0.002706 | -0.09989 | -0.02094 | 0.004356 |
| GSK3ALPHABETA | -0.061173712 | 0.004661 | -0.10354 | -0.01881 | 0.007324 |
| P27\_pT157 | -0.062433589 | 0.004799 | -0.10582 | -0.01905 | 0.007482 |
| TIGAR | -0.062784371 | 0.000271 | -0.09657 | -0.029 | 0.000516 |
| CLAUDIN7 | -0.062923995 | 0.000349 | -0.0974 | -0.02845 | 0.000652 |
| X1433EPSILON | -0.063814884 | 0.000493 | -0.0997 | -0.02793 | 0.000887 |
| SMAD3 | -0.065372281 | 0.002598 | -0.10791 | -0.02284 | 0.004251 |
| CHK2 | -0.065388522 | 0.000647 | -0.10295 | -0.02783 | 0.001144 |
| PI3KP85 | -0.068317035 | 0.002579 | -0.11274 | -0.0239 | 0.004251 |
| IRS1 | -0.071832507 | 0.001021 | -0.11468 | -0.02898 | 0.001743 |
| AMPKALPHA | -0.072027069 | 9.85E-05 | -0.10826 | -0.03579 | 0.000205 |
| SMAD4 | -0.07603384 | 0.00058 | -0.11933 | -0.03273 | 0.001035 |
| PKCALPHA\_pS657 | -0.077424863 | 1.29E-07 | -0.10614 | -0.04871 | 4.26E-07 |
| MYH11 | -0.077582111 | 3.52E-05 | -0.11432 | -0.04084 | 7.75E-05 |
| AKT | -0.077926685 | 0.000409 | -0.12113 | -0.03472 | 0.000743 |
| HER3 | -0.079157984 | 0.000383 | -0.12283 | -0.03549 | 0.000709 |
| ETS1 | -0.081729648 | 0.000208 | -0.1249 | -0.03856 | 0.000403 |
| CIAP | -0.082533533 | 0.000296 | -0.12722 | -0.03784 | 0.000559 |
| RICTOR | -0.085128638 | 3.48E-06 | -0.12106 | -0.0492 | 9.56E-06 |
| PKCALPHA | -0.088074497 | 8.25E-10 | -0.11616 | -0.05999 | 3.55E-09 |
| CHK1\_pS345 | -0.088852272 | 3.34E-05 | -0.1308 | -0.0469 | 7.42E-05 |
| CD20 | -0.089732649 | 8.02E-06 | -0.1291 | -0.05036 | 1.99E-05 |
| XBP1 | -0.090988558 | 0.000101 | -0.13685 | -0.04513 | 0.000209 |
| ACC\_pS79 | -0.092591038 | 2.01E-05 | -0.13513 | -0.05005 | 4.69E-05 |
| JNK\_pT183Y185 | -0.093673548 | 1.61E-06 | -0.13192 | -0.05543 | 4.83E-06 |
| PDK1\_pS241 | -0.094291395 | 1.77E-05 | -0.13733 | -0.05125 | 4.18E-05 |
| CD31 | -0.095107576 | 6.59E-06 | -0.13645 | -0.05377 | 1.65E-05 |
| COLLAGENVI | -0.095741533 | 5.32E-06 | -0.13694 | -0.05454 | 1.37E-05 |
| GAB2 | -0.096429265 | 1.98E-08 | -0.13006 | -0.0628 | 7.67E-08 |
| ATM | -0.097059759 | 1.76E-05 | -0.14134 | -0.05278 | 4.18E-05 |
| NRAS | -0.097661553 | 1.38E-05 | -0.14166 | -0.05366 | 3.32E-05 |
| PKCPANBETAII\_pS660 | -0.098907855 | 2.41E-08 | -0.13362 | -0.0642 | 9.19E-08 |
| ERCC1 | -0.099033547 | 4.31E-06 | -0.14124 | -0.05683 | 1.14E-05 |
| SHC\_pY317 | -0.100201589 | 6.25E-06 | -0.14365 | -0.05676 | 1.59E-05 |
| SCD1 | -0.10206489 | 4.12E-06 | -0.14547 | -0.05866 | 1.10E-05 |
| PI3KP110ALPHA | -0.10470604 | 8.27E-08 | -0.14295 | -0.06646 | 2.87E-07 |
| BECLIN | -0.104777739 | 2.79E-06 | -0.14857 | -0.06098 | 7.99E-06 |
| SRC\_pY527 | -0.109117585 | 1.76E-06 | -0.15383 | -0.0644 | 5.19E-06 |
| FOXO3A | -0.109910672 | 3.67E-06 | -0.15641 | -0.06341 | 9.94E-06 |
| ARID1A | -0.11160857 | 0.000752 | -0.17648 | -0.04673 | 0.001318 |
| PKCDELTA\_pS664 | -0.112588727 | 3.28E-15 | -0.14054 | -0.08464 | 2.32E-14 |
| BRAF | -0.115399119 | 1.05E-07 | -0.15789 | -0.07291 | 3.52E-07 |
| TUBERIN\_pT1462 | -0.115686128 | 5.19E-09 | -0.15446 | -0.07691 | 2.10E-08 |
| STAT5ALPHA | -0.117692306 | 8.28E-08 | -0.16068 | -0.0747 | 2.87E-07 |
| P70S6K\_pT389 | -0.117916002 | 2.17E-11 | -0.15239 | -0.08344 | 1.10E-10 |
| FOXO3A\_pS318S321 | -0.118201814 | 4.02E-07 | -0.16388 | -0.07253 | 1.28E-06 |
| BRCA2 | -0.119140292 | 9.86E-08 | -0.16291 | -0.07537 | 3.37E-07 |
| TTF1 | -0.121621504 | 2.06E-05 | -0.17752 | -0.06572 | 4.74E-05 |
| X1433BETA | -0.124657259 | 6.99E-09 | -0.1668 | -0.08251 | 2.77E-08 |
| AMPK\_pT172 | -0.128192444 | 4.99E-08 | -0.17424 | -0.08215 | 1.83E-07 |
| CKIT | -0.131497695 | 3.90E-13 | -0.16694 | -0.09606 | 2.14E-12 |
| EEF2K | -0.133711992 | 2.92E-09 | -0.17781 | -0.08961 | 1.23E-08 |
| ADAR1 | -0.137428156 | 3.33E-06 | -0.19527 | -0.07959 | 9.29E-06 |
| RAPTOR | -0.137558995 | 4.41E-10 | -0.18072 | -0.0944 | 1.99E-09 |
| KU80 | -0.137792675 | 2.13E-10 | -0.18026 | -0.09533 | 1.06E-09 |
| RAD50 | -0.141303607 | 2.82E-10 | -0.18515 | -0.09746 | 1.34E-09 |
| SF2 | -0.141772321 | 6.08E-10 | -0.18662 | -0.09693 | 2.68E-09 |
| X53BP1 | -0.147251647 | 1.79E-12 | -0.18812 | -0.10638 | 9.59E-12 |
| PR | -0.149449125 | 1.03E-15 | -0.18588 | -0.11302 | 7.84E-15 |
| SMAC | -0.153396609 | 1.91E-11 | -0.19812 | -0.10868 | 9.94E-11 |
| MSH2 | -0.154637101 | 1.79E-13 | -0.19572 | -0.11355 | 1.04E-12 |
| DIRAS3 | -0.156887822 | 1.08E-13 | -0.19819 | -0.11558 | 6.67E-13 |
| TUBERIN | -0.157098967 | 4.60E-16 | -0.19493 | -0.11927 | 3.80E-15 |
| PARP1 | -0.15776535 | 5.57E-05 | -0.23431 | -0.08122 | 0.000117 |
| JNK2 | -0.157966059 | 6.93E-14 | -0.19923 | -0.1167 | 4.42E-13 |
| BAP1C4 | -0.162287604 | 1.43E-13 | -0.20523 | -0.11935 | 8.55E-13 |
| ANNEXINVII | -0.163607432 | 6.48E-15 | -0.20466 | -0.12255 | 4.42E-14 |
| PTEN | -0.167843707 | 2.95E-13 | -0.21285 | -0.12284 | 1.67E-12 |
| JAB1 | -0.173725443 | 0.000212 | -0.26547 | -0.08199 | 0.000407 |
| PREX1 | -0.17661382 | 9.45E-23 | -0.21176 | -0.14147 | 1.34E-21 |
| P27 | -0.177195942 | 9.50E-16 | -0.22033 | -0.13406 | 7.52E-15 |
| ERALPHA\_pS118 | -0.177923042 | 1.16E-20 | -0.21523 | -0.14062 | 1.35E-19 |
| AR | -0.187617888 | 7.94E-38 | -0.21606 | -0.15918 | 1.96E-36 |
| PDCD4 | -0.188413184 | 2.37E-17 | -0.23189 | -0.14494 | 2.24E-16 |
| MTOR\_pS2448 | -0.18862126 | 4.84E-18 | -0.23122 | -0.14603 | 4.80E-17 |
| MTOR | -0.200086045 | 2.54E-19 | -0.2436 | -0.15657 | 2.65E-18 |
| XRCC1 | -0.206403761 | 1.08E-21 | -0.24855 | -0.16426 | 1.42E-20 |
| GATA3 | -0.208899841 | 3.07E-43 | -0.2384 | -0.1794 | 8.67E-42 |
| DJ1 | -0.214494393 | 2.27E-21 | -0.25865 | -0.17034 | 2.81E-20 |
| BIM | -0.215727665 | 8.35E-24 | -0.25761 | -0.17384 | 1.27E-22 |
| INPP4B | -0.22387964 | 1.46E-26 | -0.26486 | -0.1829 | 2.41E-25 |
| ERALPHA | -0.229056851 | 8.73E-52 | -0.25847 | -0.19964 | 3.46E-50 |
| BCL2 | -0.29640499 | 7.01E-53 | -0.33405 | -0.25876 | 3.47E-51 |

**Supplementary Table S5** miRNAs associated with hypoxia gene expression phenotypes in pan-cancer analysis. Positive coefficients indicate induced by hypoxia and negative coefficients indicate hypoxia repression.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Coefficient | P-value | 2.5% CI | 97.5% CI | FDR |
| hsa-miR-210-3p | 0.5714 | 6.10E-278 | 0.541028 | 0.601772 | 4.43E-275 |
| hsa-miR-210-5p | 0.518647 | 1.82E-205 | 0.486244 | 0.55105 | 6.61E-203 |
| hsa-miR-6087 | 0.403622 | 2.19E-114 | 0.369301 | 0.437943 | 3.97E-112 |
| hsa-miR-31-3p | 0.307709 | 3.15E-81 | 0.27642 | 0.338997 | 3.27E-79 |
| hsa-miR-21-3p | 0.307562 | 5.75E-132 | 0.283295 | 0.331828 | 1.39E-129 |
| hsa-miR-31-5p | 0.305848 | 3.27E-77 | 0.273914 | 0.337781 | 2.97E-75 |
| hsa-miR-27a-3p | 0.298303 | 5.79E-88 | 0.269206 | 0.327399 | 7.01E-86 |
| hsa-miR-24-3p | 0.29693 | 3.72E-77 | 0.265916 | 0.327944 | 3.00E-75 |
| hsa-miR-24-2-5p | 0.272201 | 5.96E-62 | 0.240315 | 0.304086 | 3.33E-60 |
| hsa-miR-455-3p | 0.258951 | 2.11E-53 | 0.226166 | 0.291736 | 9.01E-52 |
| hsa-miR-223-3p | 0.257484 | 1.45E-49 | 0.223585 | 0.291383 | 5.53E-48 |
| hsa-miR-224-5p | 0.256464 | 1.94E-66 | 0.227501 | 0.285428 | 1.28E-64 |
| hsa-miR-23a-3p | 0.251531 | 1.98E-62 | 0.222185 | 0.280877 | 1.20E-60 |
| hsa-miR-2355-3p | 0.243147 | 6.01E-38 | 0.206302 | 0.279992 | 1.51E-36 |
| hsa-miR-21-5p | 0.224481 | 4.78E-96 | 0.203568 | 0.245395 | 6.95E-94 |
| hsa-miR-23a-5p | 0.219159 | 6.29E-35 | 0.184459 | 0.253859 | 1.31E-33 |
| hsa-miR-452-5p | 0.217421 | 4.62E-47 | 0.188006 | 0.246835 | 1.68E-45 |
| hsa-miR-1293 | 0.21228 | 1.30E-40 | 0.181245 | 0.243315 | 3.77E-39 |
| hsa-miR-222-3p | 0.210873 | 1.83E-45 | 0.181822 | 0.239925 | 6.06E-44 |
| hsa-miR-452-3p | 0.210792 | 1.09E-38 | 0.179175 | 0.242409 | 2.83E-37 |
| hsa-miR-27a-5p | 0.208202 | 6.39E-40 | 0.177486 | 0.238919 | 1.79E-38 |
| hsa-miR-431-5p | 0.207177 | 1.38E-30 | 0.171977 | 0.242377 | 2.51E-29 |
| hsa-miR-135b-5p | 0.202313 | 2.09E-54 | 0.176948 | 0.227679 | 9.49E-53 |
| hsa-miR-7641 | 0.197028 | 2.90E-29 | 0.162755 | 0.231301 | 4.79E-28 |
| hsa-miR-455-5p | 0.188167 | 1.80E-39 | 0.16024 | 0.216095 | 4.85E-38 |
| hsa-miR-146b-5p | 0.186412 | 2.50E-36 | 0.157505 | 0.215319 | 5.86E-35 |
| hsa-miR-134-5p | 0.186041 | 8.54E-27 | 0.152116 | 0.219965 | 1.24E-25 |
| hsa-miR-146b-3p | 0.184119 | 2.27E-42 | 0.157795 | 0.210443 | 6.88E-41 |
| hsa-miR-155-5p | 0.182462 | 4.65E-33 | 0.152718 | 0.212207 | 9.13E-32 |
| hsa-miR-574-3p | 0.181311 | 1.20E-28 | 0.149411 | 0.213212 | 1.94E-27 |
| hsa-miR-221-3p | 0.180039 | 2.97E-35 | 0.151672 | 0.208405 | 6.55E-34 |
| hsa-miR-493-5p | 0.177626 | 1.51E-25 | 0.144397 | 0.210855 | 1.92E-24 |
| hsa-miR-222-5p | 0.176803 | 2.09E-32 | 0.147674 | 0.205932 | 4.00E-31 |
| hsa-miR-212-3p | 0.175692 | 2.30E-19 | 0.137502 | 0.213882 | 2.04E-18 |
| hsa-miR-4449 | 0.174454 | 3.60E-22 | 0.139224 | 0.209685 | 4.16E-21 |
| hsa-miR-106b-3p | 0.173692 | 7.56E-26 | 0.141402 | 0.205982 | 1.00E-24 |
| hsa-miR-299-5p | 0.169713 | 1.70E-21 | 0.134863 | 0.204563 | 1.81E-20 |
| hsa-miR-193b-3p | 0.169425 | 1.21E-25 | 0.137793 | 0.201058 | 1.58E-24 |
| hsa-miR-1271-5p | 0.16819 | 1.59E-20 | 0.132771 | 0.203608 | 1.53E-19 |
| hsa-miR-493-3p | 0.167932 | 5.36E-22 | 0.133875 | 0.201989 | 6.08E-21 |
| hsa-miR-1306-3p | 0.167262 | 5.58E-20 | 0.131519 | 0.203004 | 5.20E-19 |
| hsa-miR-2355-5p | 0.165644 | 1.11E-27 | 0.13596 | 0.195328 | 1.72E-26 |
| hsa-miR-409-3p | 0.16515 | 2.21E-21 | 0.131138 | 0.199162 | 2.33E-20 |
| hsa-miR-582-5p | 0.164794 | 1.29E-20 | 0.130175 | 0.199412 | 1.27E-19 |
| hsa-miR-137 | 0.164157 | 3.77E-28 | 0.135003 | 0.193311 | 5.96E-27 |
| hsa-miR-224-3p | 0.163356 | 8.31E-20 | 0.128283 | 0.19843 | 7.64E-19 |
| hsa-miR-193a-5p | 0.159473 | 6.04E-30 | 0.13207 | 0.186875 | 1.07E-28 |
| hsa-miR-382-5p | 0.159453 | 4.76E-21 | 0.126332 | 0.192574 | 4.88E-20 |
| hsa-miR-15b-3p | 0.158237 | 6.06E-23 | 0.12687 | 0.189605 | 7.22E-22 |
| hsa-miR-582-3p | 0.157496 | 3.82E-23 | 0.126422 | 0.188571 | 4.63E-22 |
| hsa-miR-1228-3p | 0.156765 | 4.24E-17 | 0.12028 | 0.193251 | 3.14E-16 |
| hsa-miR-944 | 0.156642 | 6.87E-46 | 0.135167 | 0.178117 | 2.38E-44 |
| hsa-miR-654-3p | 0.155453 | 3.71E-17 | 0.119341 | 0.191566 | 2.78E-16 |
| hsa-miR-22-5p | 0.153873 | 1.95E-19 | 0.120493 | 0.187253 | 1.75E-18 |
| hsa-miR-3922-3p | 0.152458 | 1.38E-15 | 0.115107 | 0.189809 | 9.04E-15 |
| hsa-miR-708-5p | 0.151894 | 6.83E-23 | 0.121747 | 0.182041 | 8.01E-22 |
| hsa-miR-205-5p | 0.150739 | 5.33E-55 | 0.131949 | 0.169529 | 2.58E-53 |
| hsa-miR-550a-3p | 0.150712 | 1.73E-15 | 0.113661 | 0.187764 | 1.12E-14 |
| hsa-miR-323a-3p | 0.150449 | 2.41E-19 | 0.117728 | 0.18317 | 2.11E-18 |
| hsa-miR-193b-5p | 0.149926 | 3.43E-20 | 0.118071 | 0.181781 | 3.24E-19 |
| hsa-miR-323b-3p | 0.149359 | 4.52E-17 | 0.114566 | 0.184153 | 3.32E-16 |
| hsa-miR-379-5p | 0.149298 | 2.55E-19 | 0.116804 | 0.181792 | 2.18E-18 |
| hsa-miR-99b-3p | 0.147797 | 8.37E-21 | 0.116902 | 0.178693 | 8.45E-20 |
| hsa-miR-758-3p | 0.146583 | 1.25E-16 | 0.11194 | 0.181227 | 8.72E-16 |
| hsa-miR-937-3p | 0.144427 | 5.89E-17 | 0.110657 | 0.178197 | 4.24E-16 |
| hsa-miR-324-5p | 0.14333 | 7.25E-14 | 0.105843 | 0.180816 | 4.21E-13 |
| hsa-miR-18a-3p | 0.143226 | 6.60E-19 | 0.111683 | 0.17477 | 5.58E-18 |
| hsa-miR-135b-3p | 0.143193 | 2.51E-19 | 0.112034 | 0.174351 | 2.17E-18 |
| hsa-let-7i-3p | 0.143193 | 8.86E-20 | 0.112425 | 0.173961 | 8.05E-19 |
| hsa-miR-505-3p | 0.142699 | 2.52E-15 | 0.107409 | 0.177989 | 1.59E-14 |
| hsa-miR-196a-5p | 0.141502 | 2.65E-26 | 0.115442 | 0.167563 | 3.63E-25 |
| hsa-miR-934 | 0.140738 | 1.22E-16 | 0.107486 | 0.17399 | 8.63E-16 |
| hsa-miR-496 | 0.140558 | 2.57E-14 | 0.10445 | 0.176665 | 1.53E-13 |
| hsa-miR-511-5p | 0.140463 | 2.98E-17 | 0.107933 | 0.172994 | 2.25E-16 |
| hsa-miR-125a-3p | 0.137909 | 1.95E-17 | 0.106155 | 0.169662 | 1.49E-16 |
| hsa-miR-379-3p | 0.137236 | 4.16E-12 | 0.098478 | 0.175994 | 2.06E-11 |
| hsa-miR-629-5p | 0.136365 | 5.98E-14 | 0.10082 | 0.171911 | 3.51E-13 |
| hsa-miR-214-3p | 0.136298 | 7.64E-18 | 0.105312 | 0.167284 | 6.03E-17 |
| hsa-miR-1262 | 0.135819 | 6.72E-12 | 0.097079 | 0.174559 | 3.24E-11 |
| hsa-miR-615-3p | 0.134722 | 4.26E-18 | 0.104331 | 0.165114 | 3.48E-17 |
| hsa-miR-629-3p | 0.13413 | 1.04E-14 | 0.100191 | 0.168068 | 6.29E-14 |
| hsa-miR-187-3p | 0.133563 | 2.52E-15 | 0.100532 | 0.166594 | 1.59E-14 |
| hsa-miR-214-5p | 0.132873 | 8.51E-21 | 0.105092 | 0.160654 | 8.47E-20 |
| hsa-miR-301a-5p | 0.13273 | 1.60E-13 | 0.097522 | 0.167939 | 9.22E-13 |
| hsa-miR-4772-3p | 0.130357 | 8.17E-15 | 0.097503 | 0.163211 | 5.04E-14 |
| hsa-miR-4746-5p | 0.130215 | 2.12E-14 | 0.096871 | 0.163558 | 1.28E-13 |
| hsa-miR-92b-3p | 0.130075 | 8.54E-24 | 0.104792 | 0.155357 | 1.07E-22 |
| hsa-miR-320b | 0.129965 | 1.43E-12 | 0.094039 | 0.165891 | 7.46E-12 |
| hsa-miR-18a-5p | 0.129959 | 1.05E-18 | 0.10117 | 0.158749 | 8.75E-18 |
| hsa-miR-223-5p | 0.129427 | 3.31E-12 | 0.093044 | 0.16581 | 1.67E-11 |
| hsa-miR-193a-3p | 0.128954 | 1.95E-16 | 0.098279 | 0.159629 | 1.33E-15 |
| hsa-miR-143-5p | 0.128697 | 5.10E-17 | 0.098666 | 0.158727 | 3.70E-16 |
| hsa-miR-744-3p | 0.12794 | 4.53E-11 | 0.089905 | 0.165976 | 1.98E-10 |
| hsa-miR-6509-5p | 0.127891 | 4.23E-15 | 0.096001 | 0.159781 | 2.65E-14 |
| hsa-miR-671-5p | 0.127759 | 5.41E-13 | 0.093096 | 0.162422 | 2.91E-12 |
| hsa-miR-412-5p | 0.12706 | 4.33E-11 | 0.089324 | 0.164796 | 1.92E-10 |
| hsa-miR-33b-5p | 0.126068 | 6.29E-12 | 0.09016 | 0.161977 | 3.05E-11 |
| hsa-miR-3687 | 0.125933 | 6.23E-12 | 0.090069 | 0.161797 | 3.04E-11 |
| hsa-miR-3648 | 0.12556 | 2.00E-11 | 0.088902 | 0.162218 | 9.22E-11 |
| hsa-miR-654-5p | 0.125427 | 3.71E-12 | 0.090087 | 0.160766 | 1.85E-11 |
| hsa-miR-942-5p | 0.124576 | 5.10E-15 | 0.093419 | 0.155733 | 3.17E-14 |
| hsa-miR-16-2-3p | 0.124356 | 8.48E-15 | 0.092996 | 0.155717 | 5.18E-14 |
| hsa-miR-6718-5p | 0.124276 | 8.97E-10 | 0.084556 | 0.163996 | 3.32E-09 |
| hsa-miR-369-5p | 0.123629 | 1.33E-11 | 0.087855 | 0.159404 | 6.23E-11 |
| hsa-miR-376a-3p | 0.123258 | 2.18E-10 | 0.085243 | 0.161274 | 8.99E-10 |
| hsa-miR-203b-3p | 0.123108 | 9.48E-18 | 0.095039 | 0.151176 | 7.33E-17 |
| hsa-miR-6510-3p | 0.122737 | 7.60E-16 | 0.092942 | 0.152533 | 5.03E-15 |
| hsa-miR-197-3p | 0.12245 | 2.03E-15 | 0.092269 | 0.152631 | 1.31E-14 |
| hsa-miR-3136-5p | 0.122292 | 4.55E-10 | 0.083879 | 0.160705 | 1.77E-09 |
| hsa-miR-708-3p | 0.121496 | 1.00E-16 | 0.092872 | 0.15012 | 7.14E-16 |
| hsa-miR-369-3p | 0.121452 | 5.49E-13 | 0.088491 | 0.154413 | 2.94E-12 |
| hsa-miR-203a | 0.121437 | 2.74E-21 | 0.096367 | 0.146507 | 2.85E-20 |
| hsa-miR-221-5p | 0.120694 | 2.69E-13 | 0.088372 | 0.153016 | 1.52E-12 |
| hsa-miR-127-5p | 0.119891 | 1.85E-12 | 0.086581 | 0.153202 | 9.58E-12 |
| hsa-miR-485-3p | 0.119442 | 3.14E-13 | 0.087364 | 0.15152 | 1.75E-12 |
| hsa-miR-3651 | 0.11908 | 2.87E-10 | 0.082102 | 0.156057 | 1.16E-09 |
| hsa-miR-411-5p | 0.118905 | 3.23E-12 | 0.085497 | 0.152314 | 1.64E-11 |
| hsa-miR-877-5p | 0.118763 | 3.43E-13 | 0.086816 | 0.150711 | 1.89E-12 |
| hsa-miR-3170 | 0.118579 | 4.39E-11 | 0.083352 | 0.153807 | 1.93E-10 |
| hsa-miR-7704 | 0.118182 | 7.38E-11 | 0.082653 | 0.15371 | 3.16E-10 |
| hsa-miR-421 | 0.117424 | 1.36E-09 | 0.079484 | 0.155364 | 4.88E-09 |
| hsa-miR-381-3p | 0.117378 | 4.76E-12 | 0.084136 | 0.15062 | 2.34E-11 |
| hsa-miR-3677-3p | 0.117168 | 1.01E-09 | 0.079603 | 0.154732 | 3.67E-09 |
| hsa-miR-199b-3p | 0.116837 | 1.18E-21 | 0.09294 | 0.140735 | 1.28E-20 |
| hsa-miR-199a-3p | 0.11683 | 1.13E-21 | 0.092946 | 0.140714 | 1.24E-20 |
| hsa-miR-432-5p | 0.116135 | 7.39E-11 | 0.081219 | 0.15105 | 3.16E-10 |
| hsa-miR-411-3p | 0.115219 | 4.91E-10 | 0.078959 | 0.151479 | 1.88E-09 |
| hsa-let-7i-5p | 0.115089 | 2.16E-16 | 0.08767 | 0.142507 | 1.47E-15 |
| hsa-miR-154-5p | 0.114908 | 3.47E-10 | 0.079058 | 0.150758 | 1.38E-09 |
| hsa-miR-758-5p | 0.114738 | 3.38E-12 | 0.082471 | 0.147004 | 1.69E-11 |
| hsa-miR-370-3p | 0.114313 | 1.95E-11 | 0.080958 | 0.147669 | 9.04E-11 |
| hsa-miR-127-3p | 0.113928 | 8.78E-12 | 0.08125 | 0.146607 | 4.17E-11 |
| hsa-miR-154-3p | 0.112838 | 9.09E-10 | 0.076761 | 0.148914 | 3.34E-09 |
| hsa-miR-196b-5p | 0.112391 | 8.72E-18 | 0.086795 | 0.137988 | 6.82E-17 |
| hsa-miR-6892-5p | 0.111908 | 9.91E-10 | 0.076047 | 0.147769 | 3.62E-09 |
| hsa-miR-584-5p | 0.111725 | 5.01E-13 | 0.081457 | 0.141994 | 2.72E-12 |
| hsa-miR-451a | 0.111621 | 1.18E-09 | 0.075689 | 0.147553 | 4.26E-09 |
| hsa-miR-330-5p | 0.11159 | 4.03E-10 | 0.076645 | 0.146535 | 1.58E-09 |
| hsa-miR-331-5p | 0.111215 | 1.86E-09 | 0.074975 | 0.147456 | 6.57E-09 |
| hsa-miR-589-3p | 0.110698 | 3.46E-08 | 0.071395 | 0.150001 | 1.07E-07 |
| hsa-miR-425-5p | 0.110301 | 1.44E-10 | 0.076618 | 0.143985 | 6.05E-10 |
| hsa-miR-27b-3p | 0.110134 | 7.12E-12 | 0.078683 | 0.141585 | 3.40E-11 |
| hsa-miR-766-3p | 0.110107 | 3.65E-10 | 0.075711 | 0.144502 | 1.44E-09 |
| hsa-miR-576-5p | 0.108899 | 3.47E-09 | 0.0728 | 0.144999 | 1.19E-08 |
| hsa-miR-365a-3p | 0.10876 | 3.35E-11 | 0.076644 | 0.140876 | 1.51E-10 |
| hsa-miR-365b-3p | 0.108716 | 3.42E-11 | 0.076599 | 0.140833 | 1.53E-10 |
| hsa-miR-155-3p | 0.108401 | 9.39E-09 | 0.071425 | 0.145377 | 3.10E-08 |
| hsa-miR-130b-3p | 0.107787 | 5.78E-11 | 0.075564 | 0.140011 | 2.52E-10 |
| hsa-miR-339-5p | 0.10768 | 1.91E-08 | 0.070157 | 0.145203 | 6.05E-08 |
| hsa-miR-376c-3p | 0.107549 | 5.64E-10 | 0.073583 | 0.141514 | 2.13E-09 |
| hsa-miR-4772-5p | 0.107204 | 1.14E-08 | 0.07042 | 0.143988 | 3.75E-08 |
| hsa-miR-1306-5p | 0.105641 | 3.43E-10 | 0.072693 | 0.138589 | 1.37E-09 |
| hsa-miR-324-3p | 0.105253 | 1.43E-09 | 0.071196 | 0.13931 | 5.10E-09 |
| hsa-miR-134-3p | 0.105186 | 2.19E-08 | 0.068375 | 0.141996 | 6.88E-08 |
| hsa-miR-183-3p | 0.104991 | 7.21E-10 | 0.071623 | 0.138358 | 2.70E-09 |
| hsa-miR-889-3p | 0.10379 | 1.34E-10 | 0.07215 | 0.13543 | 5.69E-10 |
| hsa-miR-132-5p | 0.103598 | 9.16E-08 | 0.065618 | 0.141578 | 2.62E-07 |
| hsa-miR-144-3p | 0.103365 | 5.27E-09 | 0.068693 | 0.138037 | 1.77E-08 |
| hsa-miR-494-3p | 0.102385 | 3.63E-08 | 0.065979 | 0.13879 | 1.12E-07 |
| hsa-miR-34c-3p | 0.102099 | 9.00E-10 | 0.069464 | 0.134734 | 3.32E-09 |
| hsa-miR-487b-3p | 0.101881 | 6.48E-09 | 0.067504 | 0.136258 | 2.16E-08 |
| hsa-miR-301a-3p | 0.101527 | 1.39E-10 | 0.070549 | 0.132504 | 5.87E-10 |
| hsa-miR-382-3p | 0.100361 | 1.01E-08 | 0.066054 | 0.134667 | 3.32E-08 |
| hsa-miR-539-5p | 0.100109 | 2.61E-08 | 0.064882 | 0.135336 | 8.14E-08 |
| hsa-miR-940 | 0.099558 | 6.20E-08 | 0.063534 | 0.135582 | 1.84E-07 |
| hsa-miR-616-3p | 0.099381 | 2.46E-07 | 0.061661 | 0.137101 | 6.77E-07 |
| hsa-miR-424-3p | 0.098105 | 1.52E-08 | 0.064152 | 0.132058 | 4.90E-08 |
| hsa-miR-28-3p | 0.098012 | 2.20E-10 | 0.067774 | 0.12825 | 9.03E-10 |
| hsa-miR-4652-5p | 0.097537 | 1.17E-08 | 0.064051 | 0.131024 | 3.81E-08 |
| hsa-miR-584-3p | 0.097196 | 1.13E-07 | 0.06131 | 0.133081 | 3.20E-07 |
| hsa-miR-548d-3p | 0.097149 | 1.10E-06 | 0.058087 | 0.13621 | 2.82E-06 |
| hsa-let-7b-5p | 0.096678 | 1.94E-09 | 0.065141 | 0.128216 | 6.80E-09 |
| hsa-miR-337-3p | 0.096446 | 1.71E-07 | 0.060317 | 0.132574 | 4.79E-07 |
| hsa-miR-132-3p | 0.096273 | 8.34E-08 | 0.06109 | 0.131456 | 2.40E-07 |
| hsa-miR-409-5p | 0.096047 | 1.76E-07 | 0.060029 | 0.132066 | 4.92E-07 |
| hsa-miR-655-3p | 0.095312 | 2.17E-08 | 0.061966 | 0.128658 | 6.85E-08 |
| hsa-miR-487a-3p | 0.095212 | 7.06E-07 | 0.057608 | 0.132817 | 1.85E-06 |
| hsa-miR-365a-5p | 0.095101 | 2.53E-08 | 0.061667 | 0.128535 | 7.94E-08 |
| hsa-miR-410-3p | 0.094565 | 3.71E-08 | 0.060915 | 0.128215 | 1.14E-07 |
| hsa-miR-590-5p | 0.094532 | 3.49E-11 | 0.066593 | 0.122471 | 1.55E-10 |
| hsa-miR-4326 | 0.094492 | 3.55E-06 | 0.054566 | 0.134419 | 8.42E-06 |
| hsa-miR-4758-3p | 0.093192 | 4.65E-09 | 0.062045 | 0.12434 | 1.58E-08 |
| hsa-miR-431-3p | 0.093033 | 1.50E-08 | 0.060852 | 0.125213 | 4.84E-08 |
| hsa-miR-151a-5p | 0.092556 | 6.69E-07 | 0.056077 | 0.129035 | 1.77E-06 |
| hsa-miR-3187-3p | 0.092435 | 7.68E-07 | 0.055806 | 0.129064 | 2.00E-06 |
| hsa-miR-1226-3p | 0.091939 | 4.56E-08 | 0.059005 | 0.124873 | 1.39E-07 |
| hsa-miR-376b-3p | 0.091215 | 6.88E-07 | 0.055226 | 0.127204 | 1.81E-06 |
| hsa-let-7f-1-3p | 0.09092 | 1.03E-07 | 0.057453 | 0.124387 | 2.94E-07 |
| hsa-miR-6842-3p | 0.090676 | 2.62E-07 | 0.056179 | 0.125174 | 7.20E-07 |
| hsa-miR-503-5p | 0.090665 | 4.96E-07 | 0.055342 | 0.125988 | 1.33E-06 |
| hsa-miR-200a-5p | 0.090236 | 4.48E-18 | 0.069866 | 0.110606 | 3.62E-17 |
| hsa-miR-495-3p | 0.090089 | 2.21E-07 | 0.056028 | 0.124149 | 6.11E-07 |
| hsa-miR-15b-5p | 0.089996 | 3.27E-09 | 0.060213 | 0.119779 | 1.13E-08 |
| hsa-miR-301b | 0.089659 | 1.07E-06 | 0.053657 | 0.125661 | 2.74E-06 |
| hsa-miR-551a | 0.08941 | 1.17E-06 | 0.053372 | 0.125449 | 2.97E-06 |
| hsa-miR-136-5p | 0.088976 | 5.50E-08 | 0.056908 | 0.121043 | 1.64E-07 |
| hsa-miR-423-3p | 0.088579 | 7.17E-08 | 0.056373 | 0.120786 | 2.10E-07 |
| hsa-miR-376c-5p | 0.088413 | 4.89E-06 | 0.050509 | 0.126318 | 1.15E-05 |
| hsa-miR-34a-5p | 0.087208 | 1.46E-07 | 0.054717 | 0.1197 | 4.12E-07 |
| hsa-miR-329-3p | 0.087022 | 1.15E-06 | 0.051972 | 0.122073 | 2.93E-06 |
| hsa-miR-376b-5p | 0.086505 | 8.86E-06 | 0.048364 | 0.124647 | 2.02E-05 |
| hsa-miR-34b-3p | 0.086036 | 7.93E-07 | 0.051899 | 0.120172 | 2.06E-06 |
| hsa-miR-522-3p | 0.085978 | 2.13E-06 | 0.050448 | 0.121508 | 5.25E-06 |
| hsa-miR-3940-3p | 0.085005 | 4.02E-06 | 0.048884 | 0.121126 | 9.46E-06 |
| hsa-miR-486-5p | 0.083795 | 8.10E-06 | 0.047008 | 0.120582 | 1.86E-05 |
| hsa-miR-1976 | 0.083059 | 1.29E-06 | 0.049455 | 0.116664 | 3.25E-06 |
| hsa-miR-17-5p | 0.082926 | 1.41E-06 | 0.049252 | 0.116599 | 3.54E-06 |
| hsa-miR-519a-5p | 0.082725 | 7.04E-07 | 0.050055 | 0.115395 | 1.85E-06 |
| hsa-miR-199a-5p | 0.082395 | 3.79E-09 | 0.055015 | 0.109774 | 1.29E-08 |
| hsa-miR-200b-5p | 0.082194 | 2.57E-13 | 0.060201 | 0.104186 | 1.46E-12 |
| hsa-miR-656-3p | 0.082094 | 6.74E-06 | 0.046367 | 0.117822 | 1.56E-05 |
| hsa-miR-105-5p | 0.081838 | 2.96E-06 | 0.047533 | 0.116142 | 7.20E-06 |
| hsa-miR-4677-3p | 0.081746 | 7.79E-08 | 0.051941 | 0.111551 | 2.26E-07 |
| hsa-miR-6720-3p | 0.081143 | 2.12E-06 | 0.047616 | 0.114669 | 5.25E-06 |
| hsa-let-7b-3p | 0.080736 | 2.26E-06 | 0.04729 | 0.114183 | 5.53E-06 |
| hsa-miR-425-3p | 0.080561 | 3.49E-06 | 0.046547 | 0.114576 | 8.31E-06 |
| hsa-miR-3605-3p | 0.080201 | 3.10E-06 | 0.046516 | 0.113885 | 7.45E-06 |
| hsa-let-7a-2-3p | 0.080105 | 2.15E-05 | 0.043164 | 0.117046 | 4.70E-05 |
| hsa-miR-377-3p | 0.080094 | 1.01E-05 | 0.044547 | 0.115641 | 2.30E-05 |
| hsa-miR-377-5p | 0.079797 | 3.72E-06 | 0.046009 | 0.113584 | 8.80E-06 |
| hsa-let-7e-5p | 0.079727 | 3.23E-06 | 0.046178 | 0.113276 | 7.76E-06 |
| hsa-miR-93-3p | 0.079178 | 8.40E-06 | 0.044357 | 0.113998 | 1.92E-05 |
| hsa-miR-380-3p | 0.078661 | 1.99E-05 | 0.042535 | 0.114787 | 4.37E-05 |
| hsa-miR-376a-5p | 0.077999 | 1.46E-05 | 0.042748 | 0.11325 | 3.24E-05 |
| hsa-miR-1269a | 0.077971 | 1.45E-05 | 0.04274 | 0.113202 | 3.24E-05 |
| hsa-miR-4662a-5p | 0.077932 | 5.31E-06 | 0.044394 | 0.11147 | 1.24E-05 |
| hsa-miR-181a-2-3p | 0.077739 | 1.80E-07 | 0.048561 | 0.106917 | 5.02E-07 |
| hsa-miR-519a-3p | 0.077482 | 1.23E-05 | 0.042764 | 0.1122 | 2.77E-05 |
| hsa-miR-424-5p | 0.077345 | 2.63E-07 | 0.047916 | 0.106775 | 7.20E-07 |
| hsa-miR-345-5p | 0.077109 | 6.21E-06 | 0.043682 | 0.110535 | 1.44E-05 |
| hsa-miR-3200-3p | 0.077052 | 1.75E-06 | 0.045474 | 0.108631 | 4.37E-06 |
| hsa-miR-142-5p | 0.07671 | 1.26E-08 | 0.050314 | 0.103106 | 4.09E-08 |
| hsa-miR-3622a-3p | 0.076637 | 5.82E-07 | 0.046595 | 0.106678 | 1.54E-06 |
| hsa-let-7a-3p | 0.076611 | 2.97E-07 | 0.04733 | 0.105891 | 8.10E-07 |
| hsa-miR-675-3p | 0.076579 | 9.40E-06 | 0.042717 | 0.110442 | 2.14E-05 |
| hsa-miR-370-5p | 0.075359 | 2.25E-05 | 0.040523 | 0.110195 | 4.90E-05 |
| hsa-miR-1248 | 0.074733 | 0.000209 | 0.035243 | 0.114223 | 0.00041 |
| hsa-miR-516a-5p | 0.074671 | 3.12E-05 | 0.03954 | 0.109802 | 6.71E-05 |
| hsa-miR-429 | 0.074067 | 1.35E-11 | 0.052627 | 0.095506 | 6.28E-11 |
| hsa-miR-590-3p | 0.073679 | 1.63E-06 | 0.043576 | 0.103781 | 4.07E-06 |
| hsa-miR-103a-2-5p | 0.073564 | 0.000218 | 0.034574 | 0.112554 | 0.000428 |
| hsa-miR-130a-5p | 0.072978 | 6.51E-05 | 0.037172 | 0.108784 | 0.000134 |
| hsa-miR-130a-3p | 0.072884 | 3.85E-05 | 0.038193 | 0.107575 | 8.13E-05 |
| hsa-miR-521 | 0.072754 | 0.000102 | 0.036059 | 0.109449 | 0.000208 |
| hsa-miR-487a-5p | 0.072512 | 3.23E-05 | 0.03833 | 0.106694 | 6.92E-05 |
| hsa-miR-1277-3p | 0.07236 | 0.000109 | 0.035712 | 0.109008 | 0.000221 |
| hsa-miR-380-5p | 0.072126 | 5.89E-05 | 0.036947 | 0.107306 | 0.000122 |
| hsa-miR-27b-5p | 0.071588 | 3.31E-05 | 0.037797 | 0.105378 | 7.06E-05 |
| hsa-miR-99b-5p | 0.07142 | 9.46E-07 | 0.042883 | 0.099957 | 2.43E-06 |
| hsa-miR-200a-3p | 0.070328 | 3.22E-10 | 0.048428 | 0.092229 | 1.29E-09 |
| hsa-miR-503-3p | 0.070168 | 5.61E-05 | 0.036042 | 0.104294 | 0.000117 |
| hsa-miR-1266-5p | 0.069758 | 1.03E-05 | 0.038768 | 0.100747 | 2.33E-05 |
| hsa-miR-543 | 0.069477 | 0.000201 | 0.03286 | 0.106094 | 0.000396 |
| hsa-miR-9-5p | 0.069073 | 5.05E-08 | 0.044248 | 0.093898 | 1.52E-07 |
| hsa-miR-152-3p | 0.068923 | 6.08E-05 | 0.035244 | 0.102602 | 0.000126 |
| hsa-miR-106b-5p | 0.068681 | 1.41E-05 | 0.037693 | 0.099669 | 3.15E-05 |
| hsa-miR-199b-5p | 0.06852 | 4.60E-08 | 0.043969 | 0.093071 | 1.39E-07 |
| hsa-miR-143-3p | 0.068482 | 1.95E-06 | 0.040288 | 0.096677 | 4.85E-06 |
| hsa-miR-484 | 0.068459 | 7.08E-05 | 0.034702 | 0.102216 | 0.000145 |
| hsa-miR-185-3p | 0.068012 | 0.000154 | 0.0328 | 0.103223 | 0.000307 |
| hsa-miR-1185-1-3p | 0.067861 | 2.61E-05 | 0.036241 | 0.099481 | 5.67E-05 |
| hsa-miR-1283 | 0.066996 | 0.000199 | 0.03171 | 0.102282 | 0.000393 |
| hsa-miR-125b-1-3p | 0.066895 | 6.92E-05 | 0.033955 | 0.099835 | 0.000142 |
| hsa-miR-299-3p | 0.066648 | 0.000305 | 0.030486 | 0.102811 | 0.000592 |
| hsa-let-7d-3p | 0.066312 | 5.64E-06 | 0.037694 | 0.094929 | 1.31E-05 |
| hsa-miR-381-5p | 0.065574 | 0.000534 | 0.028469 | 0.102679 | 0.000993 |
| hsa-miR-98-3p | 0.065557 | 0.000507 | 0.028613 | 0.102501 | 0.000954 |
| hsa-miR-4661-5p | 0.065239 | 0.000617 | 0.027901 | 0.102576 | 0.001136 |
| hsa-miR-93-5p | 0.064632 | 0.000373 | 0.02904 | 0.100223 | 0.000716 |
| hsa-miR-9-3p | 0.064016 | 4.06E-07 | 0.039265 | 0.088768 | 1.09E-06 |
| hsa-miR-200b-3p | 0.063715 | 8.07E-10 | 0.043407 | 0.084023 | 3.01E-09 |
| hsa-miR-4431 | 0.063542 | 0.000575 | 0.027379 | 0.099705 | 0.001064 |
| hsa-miR-136-3p | 0.063268 | 0.000114 | 0.031135 | 0.095402 | 0.00023 |
| hsa-miR-539-3p | 0.062485 | 0.000795 | 0.025983 | 0.098988 | 0.001456 |
| hsa-miR-767-5p | 0.062469 | 0.000332 | 0.028363 | 0.096575 | 0.000642 |
| hsa-miR-146a-3p | 0.062174 | 0.002757 | 0.021473 | 0.102875 | 0.004621 |
| hsa-miR-1307-3p | 0.061953 | 0.000127 | 0.030269 | 0.093636 | 0.000256 |
| hsa-miR-181b-5p | 0.06171 | 4.86E-05 | 0.031947 | 0.091473 | 0.000102 |
| hsa-miR-7974 | 0.061677 | 0.00111 | 0.024613 | 0.098741 | 0.001993 |
| hsa-miR-33a-5p | 0.061384 | 0.000157 | 0.029567 | 0.093201 | 0.000312 |
| hsa-let-7d-5p | 0.061047 | 0.000806 | 0.025347 | 0.096747 | 0.001471 |
| hsa-miR-1229-3p | 0.060955 | 0.000955 | 0.024796 | 0.097113 | 0.001736 |
| hsa-miR-1197 | 0.060911 | 5.04E-05 | 0.031473 | 0.090349 | 0.000105 |
| hsa-miR-550a-5p | 0.060901 | 0.001094 | 0.02435 | 0.097452 | 0.001969 |
| hsa-miR-34c-5p | 0.060216 | 0.000427 | 0.026724 | 0.093708 | 0.000814 |
| hsa-miR-149-5p | 0.060095 | 3.75E-05 | 0.031533 | 0.088658 | 7.95E-05 |
| hsa-miR-769-3p | 0.060089 | 0.001345 | 0.023362 | 0.096816 | 0.002385 |
| hsa-miR-577 | 0.059841 | 0.000171 | 0.028638 | 0.091044 | 0.00034 |
| hsa-miR-29b-1-5p | 0.059794 | 0.001623 | 0.022617 | 0.096972 | 0.002822 |
| hsa-miR-7706 | 0.059525 | 0.000589 | 0.025585 | 0.093464 | 0.001086 |
| hsa-miR-130b-5p | 0.059112 | 0.000526 | 0.025703 | 0.09252 | 0.000981 |
| hsa-miR-16-5p | 0.058343 | 0.000307 | 0.026667 | 0.090018 | 0.000596 |
| hsa-miR-186-5p | 0.05801 | 0.001247 | 0.022792 | 0.093227 | 0.002217 |
| hsa-miR-3150b-3p | 0.057583 | 0.000992 | 0.023313 | 0.091852 | 0.001791 |
| hsa-miR-365b-5p | 0.057553 | 0.000782 | 0.023977 | 0.091129 | 0.001436 |
| hsa-miR-3173-5p | 0.056992 | 0.002564 | 0.019957 | 0.094026 | 0.004334 |
| hsa-miR-541-5p | 0.056452 | 0.000494 | 0.024703 | 0.088202 | 0.000935 |
| hsa-miR-624-5p | 0.055883 | 0.003327 | 0.018579 | 0.093187 | 0.00551 |
| hsa-miR-18b-3p | 0.054232 | 0.002669 | 0.018847 | 0.089616 | 0.004491 |
| hsa-miR-760 | 0.053928 | 0.002028 | 0.019684 | 0.088172 | 0.003485 |
| hsa-miR-146a-5p | 0.053029 | 0.000518 | 0.023096 | 0.082962 | 0.00097 |
| hsa-miR-92b-5p | 0.052629 | 0.000993 | 0.021307 | 0.083952 | 0.001791 |
| hsa-miR-625-3p | 0.052373 | 0.00086 | 0.021579 | 0.083168 | 0.001567 |
| hsa-miR-142-3p | 0.052076 | 3.46E-05 | 0.027437 | 0.076715 | 7.35E-05 |
| hsa-miR-1292-5p | 0.052034 | 0.002311 | 0.018569 | 0.085499 | 0.003934 |
| hsa-miR-22-3p | 0.051697 | 0.000523 | 0.022493 | 0.080902 | 0.000977 |
| hsa-miR-144-5p | 0.051329 | 0.001691 | 0.019292 | 0.083367 | 0.00292 |
| hsa-miR-770-5p | 0.051063 | 0.002534 | 0.01792 | 0.084206 | 0.004304 |
| hsa-miR-744-5p | 0.050254 | 0.002977 | 0.017096 | 0.083411 | 0.004964 |
| hsa-miR-141-3p | 0.050231 | 2.69E-10 | 0.034658 | 0.065803 | 1.10E-09 |
| hsa-miR-3615 | 0.050143 | 0.002624 | 0.017483 | 0.082803 | 0.004425 |
| hsa-miR-1254 | 0.050139 | 0.004139 | 0.015871 | 0.084408 | 0.006658 |
| hsa-miR-551b-3p | 0.050134 | 0.00348 | 0.016508 | 0.08376 | 0.00573 |
| hsa-miR-527 | 0.04995 | 0.003676 | 0.01625 | 0.083649 | 0.005991 |
| hsa-let-7e-3p | 0.04963 | 0.001402 | 0.019183 | 0.080077 | 0.002467 |
| hsa-miR-518a-5p | 0.049282 | 0.00411 | 0.015626 | 0.082937 | 0.006625 |
| hsa-miR-323a-5p | 0.048821 | 0.002908 | 0.016687 | 0.080955 | 0.00486 |
| hsa-miR-185-5p | 0.047581 | 0.003327 | 0.015819 | 0.079343 | 0.00551 |
| hsa-miR-200c-3p | 0.046773 | 6.84E-11 | 0.032736 | 0.06081 | 2.96E-10 |
| hsa-miR-450a-5p | 0.046635 | 0.004306 | 0.014622 | 0.078649 | 0.00691 |
| hsa-miR-1301-3p | 0.046094 | 0.003628 | 0.01504 | 0.077148 | 0.005927 |
| hsa-miR-181b-3p | 0.045721 | 0.001476 | 0.01754 | 0.073901 | 0.002586 |
| hsa-miR-302c-5p | 0.044322 | 9.33E-07 | 0.026622 | 0.062022 | 2.41E-06 |
| hsa-miR-181c-3p | 0.042512 | 0.005813 | 0.012305 | 0.072719 | 0.009128 |
| hsa-miR-3613-5p | 0.041826 | 0.004491 | 0.012978 | 0.070673 | 0.007158 |
| hsa-miR-19a-3p | 0.040112 | 0.005572 | 0.011753 | 0.068472 | 0.008807 |
| hsa-miR-200c-5p | 0.034461 | 6.21E-05 | 0.017601 | 0.05132 | 0.000128 |
| hsa-miR-141-5p | 0.032018 | 1.59E-05 | 0.017484 | 0.046552 | 3.51E-05 |
| hsa-miR-122-5p | 0.028332 | 0.001219 | 0.011167 | 0.045498 | 0.002171 |
| hsa-miR-302d-5p | 0.025366 | 0.003887 | 0.008148 | 0.042583 | 0.006308 |
| hsa-miR-302c-3p | 0.021789 | 0.004708 | 0.006681 | 0.036898 | 0.007474 |
| hsa-miR-371a-3p | -0.03025 | 0.003484 | -0.05053 | -0.00996 | 0.00573 |
| hsa-miR-373-5p | -0.03218 | 0.000333 | -0.04975 | -0.01461 | 0.000643 |
| hsa-miR-373-3p | -0.03223 | 0.005722 | -0.05509 | -0.00937 | 0.009005 |
| hsa-miR-135a-3p | -0.03893 | 0.004476 | -0.06577 | -0.01209 | 0.007152 |
| hsa-miR-192-3p | -0.04215 | 0.000359 | -0.0653 | -0.019 | 0.000691 |
| hsa-miR-140-5p | -0.04364 | 0.00165 | -0.07081 | -0.01646 | 0.002856 |
| hsa-miR-1 | -0.04481 | 0.004365 | -0.07562 | -0.014 | 0.00699 |
| hsa-miR-628-5p | -0.04487 | 0.002146 | -0.07352 | -0.01622 | 0.00368 |
| hsa-miR-338-5p | -0.04502 | 0.005591 | -0.07687 | -0.01318 | 0.008817 |
| hsa-miR-513c-3p | -0.04588 | 0.003284 | -0.07647 | -0.0153 | 0.005464 |
| hsa-miR-328-3p | -0.04619 | 0.000442 | -0.07195 | -0.02043 | 0.000841 |
| hsa-miR-181c-5p | -0.0463 | 0.003761 | -0.07762 | -0.01499 | 0.006117 |
| hsa-miR-508-5p | -0.04684 | 0.001212 | -0.0752 | -0.01848 | 0.002164 |
| hsa-miR-513a-3p | -0.04697 | 0.002553 | -0.07748 | -0.01646 | 0.004326 |
| hsa-miR-338-3p | -0.04833 | 0.001381 | -0.07793 | -0.01872 | 0.002443 |
| hsa-miR-340-5p | -0.04834 | 0.001632 | -0.07841 | -0.01827 | 0.002832 |
| hsa-miR-372-5p | -0.04867 | 6.73E-08 | -0.06633 | -0.03101 | 1.98E-07 |
| hsa-miR-100-5p | -0.04891 | 0.005368 | -0.08335 | -0.01448 | 0.008503 |
| hsa-miR-378c | -0.04919 | 0.002759 | -0.08139 | -0.01699 | 0.004621 |
| hsa-miR-513b-5p | -0.04982 | 0.00161 | -0.08077 | -0.01887 | 0.002806 |
| hsa-miR-148b-3p | -0.0501 | 0.004096 | -0.0843 | -0.0159 | 0.006617 |
| hsa-let-7f-5p | -0.05058 | 0.004499 | -0.08547 | -0.01569 | 0.007158 |
| hsa-miR-502-3p | -0.05248 | 0.004002 | -0.08822 | -0.01675 | 0.006479 |
| hsa-miR-532-3p | -0.05248 | 0.001579 | -0.08503 | -0.01993 | 0.00276 |
| hsa-miR-506-3p | -0.0525 | 0.000554 | -0.08229 | -0.02271 | 0.001027 |
| hsa-miR-125b-5p | -0.05252 | 0.000407 | -0.08164 | -0.02341 | 0.000779 |
| hsa-miR-3917 | -0.05271 | 0.002222 | -0.08647 | -0.01894 | 0.0038 |
| hsa-miR-125a-5p | -0.05285 | 0.000267 | -0.08126 | -0.02444 | 0.00052 |
| hsa-miR-192-5p | -0.05309 | 9.37E-07 | -0.0743 | -0.03189 | 2.42E-06 |
| hsa-miR-95-3p | -0.05454 | 0.001955 | -0.08905 | -0.02003 | 0.003367 |
| hsa-miR-585-3p | -0.0547 | 0.003335 | -0.09122 | -0.01818 | 0.00551 |
| hsa-miR-618 | -0.05522 | 0.003617 | -0.09242 | -0.01803 | 0.005923 |
| hsa-miR-135a-5p | -0.05593 | 1.86E-05 | -0.08152 | -0.03034 | 4.09E-05 |
| hsa-miR-32-5p | -0.05636 | 1.25E-05 | -0.08163 | -0.03108 | 2.80E-05 |
| hsa-miR-4423-5p | -0.05653 | 0.002251 | -0.0928 | -0.02027 | 0.003841 |
| hsa-miR-7-1-3p | -0.05719 | 0.001177 | -0.09173 | -0.02265 | 0.002107 |
| hsa-miR-1258 | -0.0582 | 0.003534 | -0.0973 | -0.0191 | 0.005799 |
| hsa-miR-513a-5p | -0.05847 | 0.00017 | -0.08894 | -0.028 | 0.000338 |
| hsa-miR-507 | -0.0607 | 0.000244 | -0.09312 | -0.02828 | 0.000476 |
| hsa-miR-216a-3p | -0.06074 | 0.001428 | -0.09807 | -0.02341 | 0.002508 |
| hsa-miR-26a-1-3p | -0.06083 | 0.000981 | -0.097 | -0.02466 | 0.001779 |
| hsa-miR-5589-3p | -0.06258 | 3.04E-06 | -0.08884 | -0.03632 | 7.34E-06 |
| hsa-miR-128-1-5p | -0.06293 | 8.28E-05 | -0.09425 | -0.0316 | 0.000169 |
| hsa-miR-184 | -0.06319 | 0.000451 | -0.09848 | -0.02789 | 0.000856 |
| hsa-miR-4473 | -0.0633 | 0.001399 | -0.10213 | -0.02447 | 0.002467 |
| hsa-miR-374a-5p | -0.0644 | 6.53E-08 | -0.08774 | -0.04106 | 1.93E-07 |
| hsa-miR-342-3p | -0.06443 | 0.000139 | -0.09757 | -0.0313 | 0.000278 |
| hsa-miR-372-3p | -0.06446 | 2.16E-06 | -0.09112 | -0.03781 | 5.32E-06 |
| hsa-miR-374b-5p | -0.06463 | 6.66E-05 | -0.09639 | -0.03288 | 0.000137 |
| hsa-miR-153-3p | -0.06523 | 7.24E-06 | -0.09372 | -0.03675 | 1.67E-05 |
| hsa-miR-374a-3p | -0.06591 | 5.25E-10 | -0.08669 | -0.04513 | 2.00E-09 |
| hsa-miR-383-5p | -0.06695 | 1.46E-05 | -0.09721 | -0.03668 | 3.25E-05 |
| hsa-miR-194-3p | -0.06737 | 5.01E-09 | -0.08994 | -0.04481 | 1.69E-08 |
| hsa-miR-378d | -0.06868 | 0.000514 | -0.10742 | -0.02993 | 0.000965 |
| hsa-miR-1251-3p | -0.06883 | 3.64E-07 | -0.09534 | -0.04233 | 9.84E-07 |
| hsa-miR-190b | -0.06924 | 3.42E-06 | -0.09845 | -0.04003 | 8.17E-06 |
| hsa-miR-26a-2-3p | -0.07047 | 4.28E-05 | -0.1042 | -0.03673 | 9.01E-05 |
| hsa-miR-1291 | -0.0715 | 0.000504 | -0.11178 | -0.03123 | 0.000951 |
| hsa-miR-218-5p | -0.0715 | 4.61E-05 | -0.10587 | -0.03712 | 9.68E-05 |
| hsa-miR-1468-5p | -0.07307 | 3.00E-05 | -0.10737 | -0.03876 | 6.50E-05 |
| hsa-miR-32-3p | -0.07335 | 0.000108 | -0.11047 | -0.03622 | 0.000219 |
| hsa-miR-153-5p | -0.07352 | 1.32E-07 | -0.10081 | -0.04623 | 3.73E-07 |
| hsa-miR-126-3p | -0.07358 | 5.20E-07 | -0.1023 | -0.04486 | 1.39E-06 |
| hsa-miR-126-5p | -0.07371 | 1.59E-09 | -0.09762 | -0.04979 | 5.64E-09 |
| hsa-miR-194-5p | -0.0743 | 1.03E-12 | -0.09471 | -0.05389 | 5.42E-12 |
| hsa-miR-128-3p | -0.07666 | 1.99E-07 | -0.10554 | -0.04779 | 5.52E-07 |
| hsa-miR-125b-2-3p | -0.07687 | 2.36E-06 | -0.10878 | -0.04497 | 5.76E-06 |
| hsa-miR-99a-3p | -0.07733 | 1.59E-06 | -0.10889 | -0.04576 | 3.99E-06 |
| hsa-miR-5589-5p | -0.07796 | 2.23E-09 | -0.10349 | -0.05243 | 7.76E-09 |
| hsa-miR-548b-3p | -0.07997 | 7.39E-06 | -0.11492 | -0.04501 | 1.70E-05 |
| hsa-miR-548x-3p | -0.08043 | 3.18E-05 | -0.11831 | -0.04255 | 6.82E-05 |
| hsa-miR-676-3p | -0.08045 | 3.10E-05 | -0.11828 | -0.04262 | 6.68E-05 |
| hsa-miR-150-3p | -0.08102 | 2.04E-05 | -0.11828 | -0.04376 | 4.47E-05 |
| hsa-miR-3607-3p | -0.08235 | 4.02E-06 | -0.11734 | -0.04736 | 9.46E-06 |
| hsa-miR-552-5p | -0.08351 | 2.43E-09 | -0.11093 | -0.0561 | 8.40E-09 |
| hsa-miR-664a-3p | -0.08558 | 5.55E-07 | -0.11907 | -0.0521 | 1.48E-06 |
| hsa-miR-335-5p | -0.08661 | 7.35E-08 | -0.11812 | -0.05509 | 2.14E-07 |
| hsa-miR-202-5p | -0.09005 | 7.14E-09 | -0.12052 | -0.05958 | 2.37E-08 |
| hsa-miR-664b-3p | -0.09137 | 7.27E-08 | -0.1246 | -0.05813 | 2.12E-07 |
| hsa-miR-190a-5p | -0.09148 | 1.65E-08 | -0.12322 | -0.05975 | 5.28E-08 |
| hsa-miR-552-3p | -0.09168 | 2.47E-11 | -0.11857 | -0.06479 | 1.13E-10 |
| hsa-miR-150-5p | -0.09373 | 3.00E-07 | -0.12956 | -0.05789 | 8.14E-07 |
| hsa-miR-499a-3p | -0.09605 | 3.03E-06 | -0.13635 | -0.05575 | 7.34E-06 |
| hsa-let-7c-5p | -0.09857 | 1.58E-10 | -0.12873 | -0.0684 | 6.59E-10 |
| hsa-miR-500a-3p | -0.09872 | 8.19E-08 | -0.13477 | -0.06266 | 2.36E-07 |
| hsa-miR-504-5p | -0.09959 | 5.05E-08 | -0.13538 | -0.0638 | 1.52E-07 |
| hsa-miR-26a-5p | -0.10017 | 5.78E-08 | -0.13633 | -0.06401 | 1.72E-07 |
| hsa-miR-362-3p | -0.10116 | 1.82E-08 | -0.13637 | -0.06596 | 5.81E-08 |
| hsa-miR-5683 | -0.1014 | 4.06E-08 | -0.13759 | -0.06522 | 1.24E-07 |
| hsa-miR-891b | -0.1035 | 6.42E-10 | -0.13629 | -0.0707 | 2.42E-09 |
| hsa-miR-888-5p | -0.10385 | 4.67E-10 | -0.13649 | -0.07121 | 1.81E-09 |
| hsa-miR-892b | -0.10536 | 3.56E-10 | -0.13826 | -0.07247 | 1.41E-09 |
| hsa-miR-342-5p | -0.10771 | 1.08E-11 | -0.13875 | -0.07668 | 5.08E-11 |
| hsa-miR-890 | -0.10853 | 2.88E-10 | -0.14224 | -0.07483 | 1.16E-09 |
| hsa-let-7c-3p | -0.11014 | 1.87E-10 | -0.14399 | -0.07629 | 7.77E-10 |
| hsa-miR-497-5p | -0.11027 | 2.12E-09 | -0.14633 | -0.07421 | 7.40E-09 |
| hsa-miR-30c-1-3p | -0.11117 | 4.86E-09 | -0.14837 | -0.07397 | 1.64E-08 |
| hsa-let-7g-5p | -0.11237 | 4.80E-10 | -0.14771 | -0.07702 | 1.84E-09 |
| hsa-miR-195-3p | -0.11437 | 1.41E-09 | -0.15137 | -0.07738 | 5.06E-09 |
| hsa-miR-499a-5p | -0.11509 | 2.67E-08 | -0.15562 | -0.07456 | 8.30E-08 |
| hsa-miR-140-3p | -0.11573 | 3.17E-11 | -0.14986 | -0.0816 | 1.44E-10 |
| hsa-miR-892a | -0.1166 | 2.98E-12 | -0.14931 | -0.08389 | 1.53E-11 |
| hsa-miR-30b-5p | -0.11905 | 8.84E-13 | -0.15165 | -0.08645 | 4.69E-12 |
| hsa-miR-195-5p | -0.1205 | 3.16E-13 | -0.15287 | -0.08814 | 1.75E-12 |
| hsa-miR-204-5p | -0.12438 | 2.64E-16 | -0.15409 | -0.09466 | 1.78E-15 |
| hsa-miR-6715b-3p | -0.12503 | 2.67E-12 | -0.16002 | -0.09003 | 1.38E-11 |
| hsa-miR-30d-3p | -0.12963 | 5.89E-16 | -0.16098 | -0.09828 | 3.93E-15 |
| hsa-miR-660-5p | -0.12984 | 1.69E-13 | -0.16432 | -0.09537 | 9.68E-13 |
| hsa-miR-892c-3p | -0.12997 | 4.68E-14 | -0.16371 | -0.09624 | 2.77E-13 |
| hsa-miR-532-5p | -0.13703 | 4.40E-13 | -0.17406 | -0.1 | 2.40E-12 |
| hsa-miR-1179 | -0.14872 | 1.10E-21 | -0.17911 | -0.11832 | 1.23E-20 |
| hsa-miR-30b-3p | -0.15003 | 6.33E-18 | -0.18406 | -0.11601 | 5.05E-17 |
| hsa-miR-30e-5p | -0.15367 | 1.39E-29 | -0.18025 | -0.12709 | 2.41E-28 |
| hsa-miR-362-5p | -0.15601 | 1.37E-16 | -0.19294 | -0.11909 | 9.52E-16 |
| hsa-miR-664a-5p | -0.159 | 1.55E-20 | -0.19248 | -0.12553 | 1.50E-19 |
| hsa-miR-29c-3p | -0.16352 | 8.28E-31 | -0.1912 | -0.13585 | 1.54E-29 |
| hsa-miR-30d-5p | -0.16675 | 1.39E-26 | -0.19729 | -0.13622 | 1.94E-25 |
| hsa-miR-1275 | -0.16907 | 1.73E-18 | -0.20677 | -0.13138 | 1.43E-17 |
| hsa-miR-99a-5p | -0.17014 | 2.87E-27 | -0.20088 | -0.1394 | 4.26E-26 |
| hsa-miR-29b-2-5p | -0.17212 | 5.77E-26 | -0.20403 | -0.1402 | 7.76E-25 |
| hsa-miR-7-2-3p | -0.17309 | 1.38E-35 | -0.20023 | -0.14596 | 3.13E-34 |
| hsa-miR-101-5p | -0.17347 | 1.48E-27 | -0.20463 | -0.14231 | 2.25E-26 |
| hsa-miR-30a-3p | -0.17365 | 2.11E-36 | -0.20055 | -0.14675 | 5.12E-35 |
| hsa-miR-6715a-3p | -0.1743 | 1.27E-26 | -0.2062 | -0.14241 | 1.81E-25 |
| hsa-miR-30c-2-3p | -0.17916 | 3.61E-35 | -0.20742 | -0.15089 | 7.72E-34 |
| hsa-miR-30e-3p | -0.18268 | 2.25E-23 | -0.21853 | -0.14683 | 2.77E-22 |
| hsa-miR-30a-5p | -0.18363 | 3.70E-44 | -0.20931 | -0.15794 | 1.17E-42 |
| hsa-miR-30c-5p | -0.18617 | 2.68E-29 | -0.21853 | -0.15381 | 4.52E-28 |
| hsa-miR-101-3p | -0.19181 | 2.39E-56 | -0.21542 | -0.1682 | 1.24E-54 |
| hsa-miR-29c-5p | -0.20375 | 8.67E-35 | -0.23608 | -0.17142 | 1.75E-33 |
| hsa-miR-139-3p | -0.23762 | 1.24E-49 | -0.26888 | -0.20636 | 4.99E-48 |
| hsa-miR-139-5p | -0.2805 | 3.07E-68 | -0.31174 | -0.24926 | 2.23E-66 |



**Supplementary Figure S1** Hypoxia gene expression phenotypes. Each plot is a cancer type from TCGA, where unsupervised clustering on 52 core hypoxia genes (row) stratified primary tumours (column) into high-hypoxia (column bar: red) and low-hypoxia phenotype (column bar: blue). In each cancer type, almost all 52 core hypoxia genes were up-regulated in the high-hypoxia tumours.

**Reference**

1. Yang L, West CML. Hypoxia gene expression signatures as predictive biomarkers for personalising radiotherapy. *Br J Radiol*. March 2018:20180036.

2. Harris BHL, Barberis A, West CML, Buffa FM. Gene Expression Signatures as Biomarkers of Tumour Hypoxia. *Clin Oncol*. 2017;27(10):547-560. doi:10.1016/j.clon.2015.07.004

3. Elvidge GP, Glenny L, Appelhoff RJ, Ratcliffe PJ, Ragoussis J, Gleadle JM. Concordant Regulation of Gene Expression by Hypoxia and 2-Oxoglutarate-dependent Dioxygenase Inhibition: THE ROLE OF HIF-1α, HIF-2α, AND OTHER PATHWAYS . *J Biol Chem* . 2006;281(22):15215-15226. doi:10.1074/jbc.M511408200

4. Aprelikova O, Wood M, Tackett S, Chandramouli GVR, Barrett JC. Role of ETS Transcription Factors in the Hypoxia-Inducible Factor-2 Target Gene Selection. *Cancer Res*. 2006;66(11):5641 LP-5647.

5. Wang V, Davis DA, Haque M, Huang LE, Yarchoan R. Differential Gene Up-Regulation by Hypoxia-Inducible Factor-1α and Hypoxia-Inducible Factor-2α in HEK293T Cells. *Cancer Res*. 2005;65(8):3299 LP-3306. http://cancerres.aacrjournals.org/content/65/8/3299.abstract.

6. Mense SM, Sengupta A, Zhou M, et al. Gene expression profiling reveals the profound upregulation of hypoxia-responsive genes in primary human astrocytes. *Physiol Genomics*. 2006;25(3):435-449.

7. Bosco MC, Puppo M, Santangelo C, et al. Hypoxia Modifies the Transcriptome of Primary Human Monocytes: Modulation of Novel Immune-Related Genes and Identification Of CC-Chemokine Ligand 20 as a New Hypoxia-Inducible Gene. *J Immunol*. 2006;177(3):1941 LP-1955.

8. Detwiller KY, Fernando NT, Segal NH, Ryeom SW, D&#039;Amore PA, Yoon SS. Analysis of Hypoxia-Related Gene Expression in Sarcomas and Effect of Hypoxia on RNA Interference of Vascular Endothelial Cell Growth Factor A. *Cancer Res*. 2005;65(13):5881 LP-5889.

9. Benita Y, Kikuchi H, Smith AD, Zhang MQ, Chung DC, Xavier RJ. An integrative genomics approach identifies Hypoxia Inducible Factor-1 (HIF-1)-target genes that form the core response to hypoxia. *Nucleic Acids Res*. 2009;37(14):4587-4602.

10. Seigneuric R, Starmans MHW, Fung G, et al. Impact of supervised gene signatures of early hypoxia on patient survival. *Radiother Oncol*. 2007;83(3):374-382.

11. Chi J-T, Wang Z, Nuyten DSA, et al. Gene Expression Programs in Response to Hypoxia: Cell Type Specificity and Prognostic Significance in Human Cancers. *PLOS Med*. 2006;3(3):e47. https://doi.org/10.1371/journal.pmed.0030047.

12. Jögi A, Vallon-Christersson J, Holmquist L, Axelson H, Borg Å, Påhlman S. Human neuroblastoma cells exposed to hypoxia: induction of genes associated with growth, survival, and aggressive behavior. *Exp Cell Res*. 2004;295(2):469-487.

13. Fardin P, Barla A, Mosci S, et al. A biology-driven approach identifies the hypoxia gene signature as a predictor of the outcome of neuroblastoma patients. *Mol Cancer*. 2010;9(1):185.

14. Fjeldbo CS, Julin CH, Lando M, et al. Integrative Analysis of DCE-MRI and Gene Expression Profiles in Construction of a Gene Classifier for Assessment of Hypoxia-Related Risk of Chemoradiotherapy Failure in Cervical Cancer. *Clin Cancer Res*. 2016;22(16):4067 LP-4076.

15. Harris AL. Hypoxia — a key regulatory factor in tumour growth. *Nat Rev Cancer*. 2002;2:38.