**Supplementary Table 1 |** Cell grouping and plasmid transfection

|  |  |
| --- | --- |
| Group | Plasmid |
| Control | model control |
| Ang-Ⅱ | TAD cell model |
| oe-NC | Negative control carrying overexpression plasmid |
| sh-NC | Negative control carrying interference plasmid |
| oeHIF1α | HIF1α overexpression plasmid |
| shHIF1α | HIF1α interference plasmid |
| oeKDM3A | KDM3A overexpression plasmid |
| shKDM3A | KDM3A interference plasmid |
| shHES1 | HES1 interference plasmid |
| oeHIF1α + oeKDM3A | HIF1α and KDM3A overexpression plasmids |
| oeHIF1α + shHES1 | HIF1α overexpression plasmid and HES1 interference plasmid |
| Ang-II + shHIF1α | TAD cell model and HIF1α interference plasmid |
| oeHIF1α + oeKDM3A + B9 | HIF1α overexpression plasmid + KDM3A overexpression plasmid + butyrylhydrazine (protein demethylase inhibitor) |

Note: HIF1α, hypoxia inducible factor 1α; KDM3A, lysine (K)-specific demethylase 3A; HES1, hairy and enhancer of split-1; NC, negative control.

**supplementary Table 2 |** Primer sequences for RT-qPCR

|  |  |
| --- | --- |
| Gene | Sequence |
| HIF1α | F: 5’-GACAATAGCTTCGCAGAATGC-3’ |
| R: 5’-TCGTAACTGGTCAGCTGTGG-3’ |
| KDM3A | F: 5’-ATGGTTTATGTGGGAATTCCC-3’ |
| R:5’-AGCAGCATATATGTGCCAAAG-3’ |
| HES1 | F: 5’-TCAGCGAGTGCATGAACGAG-3’ |
| R: 5’-CATGGCGTTGATCTGGGTCA-3’ |
| β-actin | F: 5’-TCCCTGGAGAAGAGCTATGA-3’ |
| R: 5’-GAATGTAGTTTCATGGATGCCAC-3’ |

Note: HIF1α, hypoxia inducible factor 1α; KDM3A, lysine (K)-specific demethylase 3A; HES1, hairy and enhancer of split-1

**Supplementary Table 3 |** Binding sites of HIF1α and HES1 promoter predicted using hTFtarget

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Pattern name | Source | Sequence name | Start | Stop | Strand | Score | P value | Q value | Matched motif |  |
| HIF1A |  | database | HES1\_romoter | 910 | 921 | - | 12.4697 | 0.0000333 | 0.0573 | GTGTGCGTGCGT |
| HIF1A |  | database | HES1\_romoter | 185 | 196 | - | 12.2273 | 0.0000399 | 0.0573 | GGCTGCGTGCTG |
| HIF1A |  | database | HES1\_romoter | 183 | 196 | - | 10.898 | 0.0000764 | 0.0619 | GGCTGCGTGCTGCC |
| HIF1A |  | database | HES1\_romoter | 909 | 920 | - | 10.945 | 0.0000856 | 0.22 | TGTGCGTGCGTG |
| HIF1A |  | database | HES1\_romoter | 967 | 980 | - | 10.6531 | 0.000087 | 0.0619 | GAGCACGTGCCAGG |
| HIF1A |  | database | HES1\_romoter | 908 | 921 | - | 10.5918 | 0.0000897 | 0.0619 | GTGTGCGTGCGTGT |
| HIF1A |  | database | HES1\_romoter | 992 | 1005 | - | 10.5204 | 0.0000931 | 0.0619 | GCCGGCGTGGGCGC |
| HIF1A | m-dataset-1629-3 | hTFtarget | HES1\_romoter | 699 | 714 | + | 23.2208 | 2.15E-10 | 0.000000531 | CACACACACACACACA |
| HIF1A | m-dataset-1629-3 | hTFtarget | HES1\_romoter | 909 | 924 | + | 21.2468 | 5.11E-09 | 0.00000457 | CACGCACGCACACACA |
| HIF1A | m-dataset-1629-3 | hTFtarget | HES1\_romoter | 903 | 918 | + | 20.9351 | 7.75E-09 | 0.00000457 | CTCACACACGCACGCA |
| HIF1A | m-dataset-1629-3 | hTFtarget | HES1\_romoter | 905 | 920 | + | 20.8961 | 8.25E-09 | 0.00000457 | CACACACGCACGCACA |
| HIF1A | m-dataset-1629-3 | hTFtarget | HES1\_romoter | 701 | 716 | + | 20.7662 | 1.05E-08 | 0.00000457 | CACACACACACACACC |
| HIF1A | m-dataset-1629-3 | hTFtarget | HES1\_romoter | 907 | 922 | + | 20.6883 | 1.11E-08 | 0.00000457 | CACACGCACGCACACA |
| HIF1A | m-dataset-1629-3 | hTFtarget | HES1\_romoter | 911 | 926 | + | 19.8442 | 3.44E-08 | 0.0000111 | CGCACGCACACACACA |
| HIF1A | m-dataset-1629-3 | hTFtarget | HES1\_romoter | 703 | 718 | + | 19.8052 | 3.61E-08 | 0.0000111 | CACACACACACACCCC |
| HIF1A | m-dataset-1629-3 | hTFtarget | HES1\_romoter | 695 | 710 | + | 19.6104 | 4.64E-08 | 0.0000127 | CGGACACACACACACA |
| HIF1A | m-dataset-1629-3 | hTFtarget | HES1\_romoter | 693 | 708 | + | 18.3506 | 0.000000196 | 0.0000482 | CCCGGACACACACACA |
| HIF1A | m-dataset-1633-2 | hTFtarget | HES1\_romoter | 891 | 909 | - | 19.0789 | 0.000000202 | 0.000371 | GTGTGAGTGAGTGTGTGTG |
| HIF1A | m-dataset-1633-2 | hTFtarget | HES1\_romoter | 893 | 911 | - | 18.1974 | 0.000000355 | 0.000371 | GTGTGTGAGTGAGTGTGTG |
| HIF1A | m-dataset-1633-2 | hTFtarget | HES1\_romoter | 887 | 905 | - | 18.1447 | 0.000000367 | 0.000371 | GAGTGAGTGTGTGTGCGCG |
| HIF1A | m-dataset-1629-3 | hTFtarget | HES1\_romoter | 899 | 914 | + | 17.5714 | 0.00000043 | 0.0000964 | CTCACTCACACACGCA |
| HIF1A | m-dataset-1633-2 | hTFtarget | HES1\_romoter | 895 | 913 | - | 17.6842 | 0.000000487 | 0.000371 | GCGTGTGTGAGTGAGTGTG |
| HIF1A | m-dataset-1629-3 | hTFtarget | HES1\_romoter | 885 | 900 | + | 17.3506 | 0.000000532 | 0.000106 | CGCGCGCACACACACT |
| HIF1A | m-dataset-1629-3 | hTFtarget | HES1\_romoter | 891 | 906 | + | 17.2987 | 0.00000056 | 0.000106 | CACACACACTCACTCA |
| HIF1A | m-dataset-1629-3 | hTFtarget | HES1\_romoter | 887 | 902 | + | 17.0909 | 0.000000677 | 0.000119 | CGCGCACACACACTCA |
| HIF1A | m-dataset-1633-2 | hTFtarget | HES1\_romoter | 899 | 917 | - | 17.1316 | 0.000000677 | 0.000413 | GCGTGCGTGTGTGAGTGAG |
| HIF1A | m-dataset-1629-3 | hTFtarget | HES1\_romoter | 705 | 720 | + | 16.961 | 0.000000766 | 0.000126 | CACACACACACCCCCC |
| HIF1A | m-dataset-1633-2 | hTFtarget | HES1\_romoter | 889 | 907 | - | 16.6184 | 0.000000912 | 0.000464 | GTGAGTGAGTGTGTGTGCG |
| HIF1A | m-dataset-1629-3 | hTFtarget | HES1\_romoter | 913 | 928 | + | 16.7273 | 0.000000948 | 0.000146 | CACGCACACACACATC |
| HIF1A | m-dataset-1629-3 | hTFtarget | HES1\_romoter | 895 | 910 | + | 16.6494 | 0.00000102 | 0.000148 | CACACTCACTCACACA |
| HIF1A | m-dataset-1633-2 | hTFtarget | HES1\_romoter | 903 | 921 | - | 15.8289 | 0.00000142 | 0.000562 | GTGTGCGTGCGTGTGTGAG |
| HIF1A | m-dataset-1633-2 | hTFtarget | HES1\_romoter | 897 | 915 | - | 15.7632 | 0.00000147 | 0.000562 | GTGCGTGTGTGAGTGAGTG |
| HIF1A | m-dataset-1633-2 | hTFtarget | HES1\_romoter | 885 | 903 | - | 15.0658 | 0.00000215 | 0.000728 | GTGAGTGTGTGTGCGCGCG |
| HIF1A | m-dataset-1633-2 | hTFtarget | HES1\_romoter | 612 | 630 | + | 14.75 | 0.00000253 | 0.000773 | GAGAGAGGGTAAGCGCCGG |
| HIF1A | m-dataset-1633-2 | hTFtarget | HES1\_romoter | 907 | 925 | - | 14.2632 | 0.00000326 | 0.000904 | GTGTGTGTGCGTGCGTGTG |
| HIF1A | m-dataset-1633-2 | hTFtarget | HES1\_romoter | 913 | 931 | - | 13.6184 | 0.0000045 | 0.00111 | GAGGATGTGTGTGTGCGTG |
| HIF1A | m-dataset-1633-2 | hTFtarget | HES1\_romoter | 699 | 717 | - | 13.5132 | 0.00000474 | 0.00111 | GGGTGTGTGTGTGTGTGTG |
| HIF1A | m-dataset-1633-2 | hTFtarget | HES1\_romoter | 901 | 919 | - | 13.1711 | 0.00000559 | 0.00122 | GTGCGTGCGTGTGTGAGTG |
| HIF1A | m-dataset-1633-2 | hTFtarget | HES1\_romoter | 905 | 923 | - | 12.5921 | 0.00000737 | 0.0015 | GTGTGTGCGTGCGTGTGTG |
| HIF1A | m-dataset-1633-2 | hTFtarget | HES1\_romoter | 701 | 719 | - | 12.4079 | 0.00000803 | 0.00153 | GGGGGTGTGTGTGTGTGTG |
| HIF1A | m-dataset-1634-1 | hTFtarget | HES1\_romoter | 910 | 921 | + | 12.8333 | 0.00000982 | 0.0278 | ACGCACGCACAC |
| HIF1A | m-dataset-1633-2 | hTFtarget | HES1\_romoter | 697 | 715 | - | 11.8421 | 0.0000104 | 0.00187 | GTGTGTGTGTGTGTGTGTC |
| HIF1A | m-dataset-1629-2 | hTFtarget | HES1\_romoter | 408 | 423 | - | 13.5065 | 0.000011 | 0.00719 | GCCCCCGCCCTCTCCC |
| HIF1A | m-dataset-1629-2 | hTFtarget | HES1\_romoter | 282 | 297 | - | 13.4675 | 0.0000113 | 0.00719 | CCGCCCGCCCCTTCCC |
| HIF1A | m-dataset-1629-2 | hTFtarget | HES1\_romoter | 610 | 625 | - | 13.4026 | 0.0000119 | 0.00719 | GCTTACCCTCTCTCCC |
| HIF1A | m-dataset-1629-2 | hTFtarget | HES1\_romoter | 1531 | 1546 | + | 13.2987 | 0.000013 | 0.00719 | TCCCCCCCTCCCCCCG |
| HIF1A | m-dataset-1629-2 | hTFtarget | HES1\_romoter | 410 | 425 | - | 13.2208 | 0.0000138 | 0.00719 | TCGCCCCCGCCCTCTC |
| HIF1A | m-dataset-1629-2 | hTFtarget | HES1\_romoter | 1084 | 1099 | - | 13.2208 | 0.0000138 | 0.00719 | CCTCTCCCTCCTCGCC |
| HIF1A | m-dataset-1633-2 | hTFtarget | HES1\_romoter | 883 | 901 | - | 11.0526 | 0.0000148 | 0.0025 | GAGTGTGTGTGCGCGCGCC |
| HIF1A | m-dataset-1633-1 | hTFtarget | HES1\_romoter | 1744 | 1761 | - | 5.48684 | 0.0000191 | 0.033 | TTTGCTACTCTCCCTCTG |
| HIF1A | m-dataset-1633-1 | hTFtarget | HES1\_romoter | 610 | 627 | - | 5.38158 | 0.0000198 | 0.033 | GCGCTTACCCTCTCTCCC |
| HIF1A | m-dataset-1633-2 | hTFtarget | HES1\_romoter | 695 | 713 | - | 10.3289 | 0.0000201 | 0.00323 | GTGTGTGTGTGTGTGTCCG |
| HIF1A | m-dataset-1633-2 | hTFtarget | HES1\_romoter | 1746 | 1764 | + | 10.0132 | 0.0000229 | 0.0035 | GAGGGAGAGTAGCAAAGGG |
| HIF1A | m-dataset-1633-3 | hTFtarget | HES1\_romoter | 1682 | 1693 | + | 12.7273 | 0.0000233 | 0.0908 | AAAAGAAATAGA |
| HIF1A | m-dataset-1629-2 | hTFtarget | HES1\_romoter | 1711 | 1726 | - | 12.4935 | 0.0000243 | 0.0108 | TTTTTTTTTCTTTCCG |
| HIF1A | m-dataset-1633-2 | hTFtarget | HES1\_romoter | 909 | 927 | - | 9.31579 | 0.0000305 | 0.00443 | ATGTGTGTGTGCGTGCGTG |
| HIF1A | m-dataset-1629-2 | hTFtarget | HES1\_romoter | 1533 | 1548 | + | 11.987 | 0.0000352 | 0.0115 | CCCCCCTCCCCCCGCC |
| HIF1A | m-dataset-1629-2 | hTFtarget | HES1\_romoter | 604 | 619 | - | 11.9351 | 0.0000365 | 0.0115 | CCTCTCTCCCCACCCC |
| HIF1A | m-dataset-1629-2 | hTFtarget | HES1\_romoter | 858 | 873 | + | 11.9221 | 0.0000368 | 0.0115 | CCGCCCCCCGCCTCCC |
| HIF1A | m-dataset-1629-3 | hTFtarget | HES1\_romoter | 917 | 932 | + | 11.5974 | 0.0000403 | 0.00552 | CACACACACATCCTCC |
| HIF1A | m-dataset-1629-3 | hTFtarget | HES1\_romoter | 879 | 894 | + | 11.4935 | 0.0000428 | 0.00555 | CCGGGGCGCGCGCACA |
| HIF1A | m-dataset-1633-1 | hTFtarget | HES1\_romoter | 900 | 917 | + | 2.97368 | 0.0000438 | 0.0486 | TCACTCACACACGCACGC |
| HIF1A | m-dataset-1629-2 | hTFtarget | HES1\_romoter | 12 | 27 | - | 11.6623 | 0.0000442 | 0.0118 | GCCTCCTCCGCCTCCC |
| HIF1A | m-dataset-1629-2 | hTFtarget | HES1\_romoter | 404 | 419 | - | 11.6234 | 0.0000454 | 0.0118 | CCGCCCTCTCCCCGCG |
| HIF1A | m-dataset-1629-3 | hTFtarget | HES1\_romoter | 697 | 712 | + | 11.3247 | 0.0000472 | 0.00582 | GACACACACACACACA |
| HIF1A | m-dataset-1633-2 | hTFtarget | HES1\_romoter | 408 | 426 | + | 8.10526 | 0.0000488 | 0.00677 | GGGAGAGGGCGGGGGCGAG |
| HIF1A | m-dataset-1634-1 | hTFtarget | HES1\_romoter | 969 | 980 | + | 11.4697 | 0.000056 | 0.0636 | TGGCACGTGCTC |
| HIF1A | m-dataset-1629-2 | hTFtarget | HES1\_romoter | 834 | 849 | + | 11.039 | 0.0000674 | 0.0162 | GCCCCCGCTCTCCGCC |
| HIF1A | m-dataset-1634-1 | hTFtarget | HES1\_romoter | 185 | 196 | + | 11.303 | 0.0000674 | 0.0636 | CAGCACGCAGCC |
| HIF1A | m-dataset-1633-3 | hTFtarget | HES1\_romoter | 1713 | 1724 | + | 10.8442 | 0.0000715 | 0.139 | GAAAGAAAAAAA |
| HIF1A | m-dataset-1629-3 | hTFtarget | HES1\_romoter | 716 | 731 | + | 10.4805 | 0.0000753 | 0.00884 | CCCCCACACGCAGCGC |
| HIF1A | m-dataset-1629-3 | hTFtarget | HES1\_romoter | 877 | 892 | + | 10.1299 | 0.0000906 | 0.0102 | CCCCGGGGCGCGCGCA |
| HIF1A | m-dataset-1629-2 | hTFtarget | HES1\_romoter | 1529 | 1544 | + | 10.5455 | 0.0000928 | 0.0198 | CGTCCCCCCCTCCCCC |
| HIF1A | m-dataset-1629-2 | hTFtarget | HES1\_romoter | 1528 | 1543 | + | 10.5065 | 0.0000951 | 0.0198 | CCGTCCCCCCCTCCCC |