**SUPPLEMENTARY DATA**

**Table S1.** miRNA predicted to regulate *VEGF-A*

|  |  |  |
| --- | --- | --- |
| Strong (44) | Weak (64) | Predicted (87) |
|  hsa-miR-101-3p |  hsa-miR-1252-3p |  hsa-miR-17-5p |
|  hsa-miR-106a-5p |  hsa-miR-1277-5p |  hsa-miR-20a-5p |
|  hsa-miR-106b-5p |  hsa-miR-1293 |  hsa-miR-93-5p |
|  hsa-miR-107 |  hsa-miR-141-5p |  hsa-miR-29b-2-5p |
|  hsa-miR-125a-5p |  hsa-miR-297 |  hsa-miR-197-5p |
|  hsa-miR-126-3p |  hsa-miR-299-3p |  hsa-miR-150-5p |
|  hsa-miR-133a-3p |  hsa-miR-29c-3p |  hsa-miR-34b-5p |
|  hsa-miR-134-5p |  hsa-miR-3163 |  hsa-miR-330-3p |
|  hsa-miR-140-5p |  hsa-miR-329-3p |  hsa-miR-328-5p |
|  hsa-miR-145-5p |  hsa-miR-335-5p |  hsa-miR-20b-5p |
|  hsa-miR-147a |  hsa-miR-362-3p |  hsa-miR-520g-3p |
|  hsa-miR-150-5p |  hsa-miR-363-5p |  hsa-miR-504-5p |
|  hsa-miR-15a-5p |  hsa-miR-3646 |  hsa-miR-638 |
|  hsa-miR-15b-5p |  hsa-miR-3662 |  hsa-miR-874-5p |
|  hsa-miR-16-5p |  hsa-miR-369-3p |  hsa-miR-541-5p |
|  hsa-miR-17-5p |  hsa-miR-374a-5p |  hsa-miR-939-5p |
|  hsa-miR-185-5p |  hsa-miR-374b-3p |  hsa-miR-1238-5p |
|  hsa-miR-195-5p |  hsa-miR-374b-5p |  hsa-miR-1285-3p |
|  hsa-miR-199a-5p |  hsa-miR-3924 |  hsa-miR-1249-5p |
|  hsa-miR-200b-3p |  hsa-miR-3941 |  hsa-miR-548o-3p |
|  hsa-miR-200c-3p |  hsa-miR-410-3p |  hsa-miR-1976 |
|  hsa-miR-203a-3p |  hsa-miR-423-3p |  hsa-miR-3122 |
|  hsa-miR-205-5p |  hsa-miR-424-5p |  hsa-miR-3132 |
|  hsa-miR-20a-5p |  hsa-miR-4263 |  hsa-miR-3175 |
|  hsa-miR-20b-5p |  hsa-miR-4483 |  hsa-miR-3184-3p |
|  hsa-miR-21-5p |  hsa-miR-4497 |  hsa-miR-4298 |
|  hsa-miR-29a-3p |  hsa-miR-451b |  hsa-miR-3650 |
|  hsa-miR-29b-3p |  hsa-miR-4524a-5p |  hsa-miR-3667-3p |
|  hsa-miR-302d-3p |  hsa-miR-4524b-5p |  hsa-miR-3922-3p |
|  hsa-miR-330-3p |  hsa-miR-4719 |  hsa-miR-550b-2-5p |
|  hsa-miR-34a-5p |  hsa-miR-4735-5p |  hsa-miR-4441 |
|  hsa-miR-34b-3p |  hsa-miR-4789-5p |  hsa-miR-4459 |
|  hsa-miR-361-5p |  hsa-miR-495-3p |  hsa-miR-4534 |
|  hsa-miR-372-3p |  hsa-miR-497-5p |  hsa-miR-3973 |
|  hsa-miR-373-3p |  hsa-miR-5193 |  hsa-miR-4632-5p |
|  hsa-miR-378a-3p |  hsa-miR-567 |  hsa-miR-4644 |
|  hsa-miR-383-5p |  hsa-miR-568 |  hsa-miR-4657 |
|  hsa-miR-503-5p |  hsa-miR-5682 |  hsa-miR-4667-5p |
|  hsa-miR-504-5p |  hsa-miR-5688 |  hsa-miR-4685-5p |
|  hsa-miR-520g-3p |  hsa-miR-5692a |  hsa-miR-4725-5p |
|  hsa-miR-520h |  hsa-miR-5692b |  hsa-miR-4728-5p |
|  hsa-miR-718 |  hsa-miR-5692c |  hsa-miR-4730 |
|  hsa-miR-93-5p |  hsa-miR-5694 |  hsa-miR-4739 |
|  hsa-miR-9-5p |  hsa-miR-576-5p |  hsa-miR-4743-3p |
|  |  hsa-miR-598-5p |  hsa-miR-4746-3p |
|  |  hsa-miR-603 |  hsa-miR-4753-3p |
|  |  hsa-miR-646 |  hsa-miR-4756-5p |
|  |  hsa-miR-660-3p |  hsa-miR-4769-5p |
|  |  hsa-miR-670-5p |  hsa-miR-5002-5p |
|  |  hsa-miR-6745 |  hsa-miR-5189-5p |
|  |  hsa-miR-6748-5p |  hsa-miR-5196-5p |
|  |  hsa-miR-6756-5p |  hsa-miR-5591-5p |
|  |  hsa-miR-6759-5p |  hsa-miR-5699-3p |
|  |  hsa-miR-6766-5p |  hsa-miR-6072 |
|  |  hsa-miR-6769a-5p |  hsa-miR-6729-5p |
|  |  hsa-miR-6769b-5p |  hsa-miR-6731-5p |
|  |  hsa-miR-6793-5p |  hsa-miR-6753-5p |
|  |  hsa-miR-6838-5p |  hsa-miR-6754-5p |
|  |  hsa-miR-6870-3p |  hsa-miR-6774-5p |
|  |  hsa-miR-6871-3p |  hsa-miR-6777-5p |
|  |  hsa-miR-7-1-3p |  hsa-miR-6785-5p |
|  |  hsa-miR-7-2-3p |  hsa-miR-6791-5p |
|  |  hsa-miR-8485 |  hsa-miR-6795-5p |
|  |  hsa-miR-95-5p |  hsa-miR-6797-5p |
|  |  |  hsa-miR-6806-3p |
|  |  |  hsa-miR-6809-3p |
|  |  |  hsa-miR-6818-3p |
|  |  |  hsa-miR-6825-5p |
|  |  |  hsa-miR-6827-5p |
|  |  |  hsa-miR-6830-3p |
|  |  |  hsa-miR-6832-5p |
|  |  |  hsa-miR-6848-3p |
|  |  |  hsa-miR-6852-5p |
|  |  |  hsa-miR-6856-5p |
|  |  |  hsa-miR-6860 |
|  |  |  hsa-miR-6873-3p |
|  |  |  hsa-miR-6875-3p |
|  |  |  hsa-miR-6876-5p |
|  |  |  hsa-miR-6879-3p |
|  |  |  hsa-miR-6887-5p |
|  |  |  hsa-miR-7107-3p |
|  |  |  hsa-miR-7112-5p |
|  |  |  hsa-miR-7156-5p |
|  |  |  hsa-miR-7160-3p |
|  |  |  hsa-miR-7851-3p |
|  |  |  hsa-miR-8085 |
|  |  |  hsa-miR-8089 |

**Table S2.** TargetScan score calculation to miRNA-mRNA binding sites within *VEGF-A*

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| miRNA | Position | Seed match | Context++  | Context++ (%) | Weight | Conservation | Pct |
| hsa-miR-29a-3p | 1758-1765 | 8mer | -0.61 |  99 | -0.46 | 4.186 | 0.89 |
| hsa-miR-29b-3p | 1758-1765 | 8mer | -0.61 |  99 | -0.46 | 4.186 | 0.89 |
| hsa-miR-15b-5p | 292-299 | 8mer | -0.51 |  99 | -0.51 | 3.981 | 0.82 |
| hsa-miR-16-5p | 292-299 | 8mer | -0.55 |  99 | -0.55 | 3.981 | 0.82 |
| hsa-miR-195-5p | 292-299 | 8mer | -0.55 |  99 | -0.55 | 3.981 | 0.82 |

**Table S3.** Gene aliases and names

|  |  |
| --- | --- |
| GENE | NAME |
| AKT2 | AKT serine/threonine kinase 2 |
| AKT3 | AKT serine/threonine kinase 3 |
| AXIN2 | Axin 2 |
| BIRC5 | Baculoviral IAP repeat containing 5 |
| FGF2 | Fibroblast growth factor 2 |
| FGFR1 | Fibroblast growth factor receptor 1 |
| FOS | Proto-oncogene, AP-1 transcription factor subunit |
| GSK3B | Glycogen synthase kinase 3 beta |
| JAG1 | Jagged canonical Notch ligand 1 |
| KDR | Kinase insert domain receptor |
| KRAS | KRAS proto-oncogene, GTPase (KRAS) |
| NOTCH2 | notch receptor 2 |
| PDGFA | platelet derived growth factor subunit A |
| PDGFB | platelet derived growth factor subunit B  |
| PDGFC | platelet derived growth factor C |
| PDGFRA | platelet derived growth factor receptor alpha |
| PDGFRB | platelet derived growth factor receptor beta |
| PIK3CG | phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit amma |
| PIK3R1 | Homo sapiens phosphoinositide-3-kinase regulatory subunit 1 |
| RAF1 | [Raf-1 proto-oncogene, serine/threonine kinase](https://www.ncbi.nlm.nih.gov/nuccore/NM_001354689.3) |
| RASA1 | RAS p21 protein activator 1  |
| RHOB | ras homolog family member B |
| STAT3 | signal transducer and activator of transcription 3 |
| VEGFA | vascular endothelial growth factor A  |
| WNT7A | Wnt family member 7A |

**Table S4. Angiogenic pathway of differentially expressed target genes**

|  |  |
| --- | --- |
| PATHWAY | GENES |
| Angiogenesis | VEGFA,KDR, FGF2, PDGFRB, PIK3CG, PDGFRA, PDGFC, RHOB, JAG1, NOTCH2, WNT7A, FOS,  |
| Apoptosis signaling pathway (P00006) | PIK3CG, FOS |
| Hypoxia response via HIF activation (P00030) | PIK3CG |
| Cadherin signaling pathway (P00012) | WNT7A |
| Endothelin signaling pathway (P00019)  | PIK3CG |
| FGF signaling pathway (P00021) | PIK3CG, FGF2 |
| Hypoxia response via HIF activation (P00030) | PIK3CG |
| Notch signaling pathway (P00045)  | NOTCH2, JAG1 |
| PDGF signaling pathway (P00047) | PIK3CG, FOS, RHOB, PDGFRA, PDGFRB |
| VEGF signaling pathway (P00056) | PIK3CG, KDR, VEGFA |
| Wnt signaling pathway (P00057) | WNT7A |

**Table S5.** Gene expression primers

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| GENE | Ref.Seq | Product length | Fw primer sequence(5' ->3') | Rv primers sequence(5' ->3') |
| AKT2 | NM\_001243027.3 | 206 | TGCCACCATGAATGAGGTGAATA | TGCAGGCAGCGTATGACAAA |
| AKT3 | NM\_001206729.2 | 704 | TAATGGGGGCGAGCTGTTTT | AGTTACCCAGCATGCCACAA |
| AXIN2 | NM\_004655.4 | 182 | TGGCAACTCAGTAACAGCCC | AGTTCCTCTCAGCAATCGGC |
| BIRC5 | NM\_001012270.2 | 382 | ACGACCCCATGCAAAGGAAA | CTGGTAAGCCCGGGAATCAA |
| FGF2 | NM\_002006.5 | 121 | TCCACCTATAATTGGTCAAAGTGGT | CATCAGTTACCAGCTCCCCC |
| FGFR1 | NM\_023110.3 | 175 | ATTTCTGCCTTGGCCCTACC | CTAGCGCAGTCTTTGGGGAA |
| FOS | NM\_005252.4 | 875 | CAAGCGGAGACAGACCAACT | ACACACTCCATGCGTTTTGC |
| GSK3B | NM\_002093.4 | 333 | GGATTCGTCAGGAACAGGACA | TTAGCATCTGACGCTGCTGT |
| JAG1 | NM\_000214.3 | 883 | GGCCGAGGTCCTATACGTTG | ACACAAGGTTTGGCCTCACA |
| KDR | NM\_002253.4 | 123 | CGGTCAACAAAGTCGGGAGA | CAGTGCACCACAAAGACACG |
| NOTCH2 | NM\_024408.4 | 73 | CTACAGTTGTCGCTGCTTGC | GTTGGAGAGGCACTCGTTGA |
| PDGFB | NM\_002608.4 | 573 | GCCAGCGCCCATTTTTCAT | GAAAAGGAACACGGCAGTCG |
| PDGFC | NM\_016205.3 | 411 | CTGCCTCTTGTTTCCAATGCC | AAGCACAGGAAAAGGGTGCT |
| PDGFRA | NM\_001347828.2 | 392 | TGTGGGACATTCATTGCGGA | GCTCACTTCCAAGACCGTCA |
| PDGFRB | NM\_002609.4 | 173 | CAAGGACACCATGCGGCTTC | AGCAGGTCAGAACGAAGGTG |
| PIK3CG | NM\_001282426.2 | 141 | TGGATATGAAGGGAGCCCCA | CATGCCCTATGCGACCTGAT |
| PIK3R1 | NM\_181504.4 | 280 | TGAGCTCAGCCAAGGAAACT | GTCCCGTCTGCTGTATCTCG |
| RAF1 | NM\_001354689.3 | 656 | ATGAGCTTGCATGACTGCCT | CAAAATCGTCTGGACCACGC |
| RASA1 | NM\_022650.3 | 606 | GGTTTCTGCTCAGCTCCCAT | TGGTGGTATTTGTAGGCCACT |
| RHOB | NM\_004040.4 | 239 | TCATGTGCTTCTCGGTGGAC | AGAGCACTCGAGGTAGTCGT |
| STAT3 | NM\_001369520.1 | 174 | TGTGACACCATTCATTGATGCAG | GTAGGCGCCTCAGTCGTATC |
| VEGFA | NM\_003376.6 | 442 | CTTGCCTTGCTGCTCTACCT | GGGATTTCTTGCGCTTTCGT |
| WNT7A | NM\_004625.4 | 505 | ACTTAGGGGTAAGGAGGGGC | GCTGGACCCAAAGCAAAGTG |

****

**Figure S1**