**Supplementary Figures and Figure Legends**

**Figure S1. Tumor histology, VHL gene sequences from specimen obtained from ccRCC patients and VHL stability test. A)** Representative images of VHL IHC of case #5, 7, 9, 11, 12 and 14, **B)** H&E stains of tumor specimen from case #17, #18, #19, #23, #24, #25 and #26 (Table I). **C)** CAM tumors of case #22 were established by implanting small tumor chunks. Images of H&E stain and VHL IHC of the CAM tumor was shown. **D)** Comparative genomic analysis of patient tumors derived cell line #22, with either the matched primary tumor tissue or control tissue from another ccRCC patient based on variant calls with an associated COSMIC ID. **E)** VHL gene sequences of ACHN, #18, #21, #22, #23 and #24 are shown. **F)**. VHL stability test upon cycloheximide (100μg/ml) treatment for 0, 3 and 6 hours and the protein level were examined by western blot in 786-O cells, with either wildtype VHL or its L169P variant overexpression. **G**) Western blot analysis of VHL, flag and HIF1A in the primary cell line from patient tumor sample #22 in either hypoxia or normoxia, and VHL knocked out #22 cells with or without VHL artificial overexpression. Flag tag is transfected with wildtype HIF1A into cells as transfection control. **H**) Western blot analysis of VHL, HIF1A and HIF2A in 786-O cells with artificial overexpression of either control vector, wildtype VHL or L169P variant. **I**) Western blot analysis of VHL, HIF1A and HIF2A in RCC-4 cells with artificial overexpression of either control vector, wildtype VHL or L169P variant. **J**) Density plot showing the copy number ratios (CNRs) of the VHL locus in the TCGA-KIRC cohort (n = 421) after adjusting for both tumor purity and ploidy with estimates from ABSOLUTE. A CNR value of -1.1 represents a two copy loss and -0.4 indicates one copy loss of VHL (dotted line). **K)** Density plot showing the variant allele frequency (VAF) of somatic VHL mutations in the TCGA-KIRC cohort after adjusting for both tumor purity and ploidy with estimates from ABSOLUTE (n = 95 cases fitting analysis criteria as described in Materials and Methods).

**Figure S2. Supplemental IHC staining and mouse weight from mice model, and the ACHN EMT changes upon VHL knockout and CAM tumor gross view from the patient #22 primary tumor derived cells. A)** A large lung metastatic lesion developed from a mouse bearing VHL-deleted RVN (RENCA, RC) renal tumor. RVN is a non-clonal selected line. The metastasis was composed predominantly of VHL+ cells with small rim of VHL-negative MMP9+ cells. **B)** Body weight of mice bearing 1:1 mixed tumor was significantly less than those bearing VHL-WT or VHL-KO tumors at 4 weeks after tumor implantation. **C)** H&E stain of lungs from a VHL-KO (clonal selected cells) tumor bearing mouse. **D)** VHL-deleted ACHN human RCC line, AC-VHL-KO cells, display EMT cell morphology compared to the parental VHL+ ACHN (AC-VHL-WT) cells. **E)** Gene expression assessed by RT-PCR showed elevated EMT markers in AC-VHL-KO cells. **F)** Gross view of the CAM tumors grown from either the original primary cancer cell line of patient #22 that’s VHL+, the derived VHL-KO cell line or the 1:1 mixture of both. (\*: p<0.05, \*\*: p<0.01)

**Figure S3. Supplemental IHC staining of Ki-67 in the lung metastasis of RENCA mouse model and the temporally sequential sampling of blood in analysis of CTC constituents.** A) IHC staining of VHL and Ki-67 in lung metastasis of mouse model which receives 1:1 mixture of VHL-WT RENCA cells and VHL-KO cells, as well as the quantification of Ki-67+ cell percentage in VHL+ and VHL- areas. B) Sequential flow cytometric analysis of circulatory tumor cells at 2, 3, 4 and 6 weeks after implantation of VHL-WT or 1:1 mixed cells. (\*\*: p<0.01)

**Figure S4. 3D migration assay of either RENCA VHL-WT cells alone, VHL-KO cells alone, or mixture of both. A)** RENCA VHL-WT cells (red), VHL-KO cells (green) or the mixture of both were observed to migrate from the top to the bottom, which was labeled as HUVECs cells (blue). The migrated distance of red cells (top left), green cells (top right), and red cells in mixture (bottom left) were quantified and analyzed (right). The video can be found in Supplemental Video 2. (\*: p<0.05, \*\*: p<0.01)

**Figure S5. POSTN expression and regulation. A)** According to TCGA RCC tumor mRNA expression database (n=532), POSTN expression is elevated in 63 cases (12%) and it is a significant poor survival indicator. **B)** POSTN expression, analyzed by RT-PCR, is elevated in RC-VHL-KO cells over VHL-WT cells. **C)** POSTN expression, analyzed by RT-PCR, is decreased by HIF1A knockout. **D)** The addition of recombinant POSTN protein enhance the motility of VHL-WT cells and Cilengitide inhibits this POSTN mediated effect. **E)** Tissue microarray (TMA) of over 300 cases of RCC patients were assessed for VHL and POSTN expression. Representative images from 16 cases showing inverse correlated expression pattern between VHL and POSTN. **F)** The tumor implanted with a 1:4 ratio of RC-VHL-WT to RC-VHL-KO cells showed robust growth of the primary tumor compared to RC-VHL-WT alone tumor. (\*\*: p<0.01; \*:P<0.05)

**Figure S6. Quantification of CTCs in the blood from mice groups received either RENCA VHL-WT cells, VHL-KO cells or mixture of both. A)** VHL-WT cells were labeled red and VHL-KO cells were labeled green. This is the endpoint blood analysis from different mice groups received RENCA cells.

**Supplementary Video Legend**

**Video 1: 2D Scratch assay for RC-VHL-WT cells alone, RC-VHL-KO cells alone, or mixture of both. A)** A scratch assay of RC-VHL-WT cells; **B)** A scratch assay of RC-VHL-KO cells; **C)** A scratch assay of mixture of both cells in a 1:1 ratio; **D)** The tritc channel of scratch assay of the mixture of both cells in 1:1 ratio.

**Video 2: 3D Scratch assay for RC-VHL-WT cells alone, RC-VHL-KO cells alone, or mixture of both. A)** A scratch assay of RC-VHL-WT cells; **B)** A scratch assay of RC-VHL-KO cells; **C)** A scratch assay of mixture of both cells in a 1:1 ratio; **D)** The tritc channel of scratch assay of the mixture of both cells in 1:1 ratio.

**Video 3: 2D Scratch assay for RC-VHL-WT cells supplemented with fresh media (A) or the conditioned media (B) from RC-VHL-KO cells.**

**Video 4: 2D Scratch assay for RC-VHL-WT cells in mixture with RC-VHL-KO cells (A) or with a compound deletion of VHL and HIF1A cells (B).**

**Video 5: 2D Scratch assay for RC-VHL-WT cells in mixture with RC-VHL-KO cells (A) or with a compound deletion of VHL and POSTN cells (B).**

**Video 6: 2D Scratch assay for RC-VHL-WT cells in mixture with RC-VHL-KO cells under the effect of control reagent PBS (A) or anti-periostin MPC4B5 mAb (B).**

**Video 7: 2D Sractch assay for RC-VHL-WT cells in mixture with RC-VHL-KO cells supplemented with Cilengitide at 0 (A), 2μM (B), 5μM(C) and 10μM (D).**

**Supplementary Methods and Materials**

**Cells, plasmids, and reagents**

The RENCA (RC) cell line was purchased from ATCC and was maintained in RPMI-1640 supplemented with 10% fetal bovine serum and 1X penicillin/streptomycin (Thermo Fisher, CA, USA, catalog number: 15140122). All CRISPR/Cas9-mediated knockout RC cell lines were selected with puromycin and clonally purified via single-cell cloning in a 96-well plate. A lentiviral vector encoding HA-tagged mStrawberry (modified from pSicoR, Addgene, MA, USA, catalog number: 11579) was used to label RC-VHL-WT cells, while a vector with the same backbone encoding flag-tagged EGFP was used to label RC-VHL-KO, RC-VHL/HIF1A-KO, and RC-VHL/POSTN-KO cells. In addition, for in vivo studies, all cell lines were also marked with lentivirus expressing firefly luciferase to permit BLI. pGL3-basic was from Promega (CA, USA, catalog number: E1751) and was enzymatically digested with MluI and XhoI. The periostin promoter was cloned from the genomic DNA of RC cells with the following primers: forward – CGACGCGTTAAGGTGGACAGTGAGGAAGACACA, reverse – CCGCTCGAGTTGAGAAGAACGAGAGTAGAGATTTTAGG. The control *renilla* luciferase vector was pRL-TK from Promega (CA, USA, catalog number: E2231). The plasmid for overexpressing constitutively-active *HIF1A* was from Addgene (MA, USA, catalog number: 44028). The wildtype VHL coding sequence was amplified from normal proximal renal tubule cells HK-2 by the following primers with EcoRV on each 5’ end: forward – AAACGGATATCATGCCCCGGAGGGCG, reverse – CGATCGATATCATCTCCCATCCGTTGATGTGC. The L169P variant is point mutated from the wildtype VHL above by relay PCR: forward 1 - AAACGGATATCATGCCCCGGAGGGCG, reverse 1 - CAGGCTTGACTGGGCTCCG; forward 2 - CGGAGCCCAGTCAAGCCTG, reverse 2 – CGATCGATATCATCTCCCATCCGTTGATGTGC. The vector backbone was from Addgene #65726, pLV-CMV-LoxP-DsRed-LoxP-eGFP.

**IHC and IF staining**

Slides were baked at 65 °C for 20 minutes and deparaffinized through three 10min incubations in xylene then rehydrated in stepwise dilutions of ethanol from 100% to 50% followed by water. Citrate buffer was used for antigen retrieval in a vegetable steamer for 25 minutes. Blocking used 1% BSA, and the following primary antibodies were incubated overnight at 4 °C: anti-VHL (1:200, Abcam, USA, catalog number: ab135576), anti-flag (1:200, eBioscience, USA, catalog number: 14-6681-82), anti-HA (1:200, Santa Cruz Biotechnology, USA, catalog number: sc805), and anti-Ki67 (1:200, Vector Laboratories, USA, catalog number: VP-RM04). After three 7-minute washes in TBST, slides were incubated with secondary antibody (goat-anti-rabbit, catalog number: 111-035-045; goat-anti-mouse, catalog number: 115-035-062; both from Jackson ImmunoResearch Laboratories, USA) at a 1:200 dilution. Slides were washed three times in TBST for 7 minutes each. For IHC, slides were incubated with DAB (Biocare Medical, USA, catalog number: DB801R) and counterstained with hematoxylin. For IF, slides were incubated with with FITC-conjugated TSA (Perkin Elmer, USA, catalog number: SAT701001EA) or CY3-conjugated TSA (Perkin Elmer, USA, catalog number: NEL744001KT). After TSA staining, Hoechst 33342 was added to the slides for nuclear staining, and slides were sealed with glycerol then scanned at UCLA’s Translational Pathology Core Laboratory (UCLA).

**qRT-PCR**

Cell mRNAs are extracted with traditional Trizol (Cat#15596026, ThermoFisher, USA) method as mentioned in Shiruyeh Schokrpur et al [1](#_ENREF_1), treated with DNase (Cat#18068015, ThermoFisher, USA) and reverse transcribed with PrimeScript 1st strand cDNA Synthesis Kit (Cat# 6110B, Takara, Japan). SensiFAST SYBR (Cat# BIO-98005, Bioline, USA) was used to for PCR reaction and signal read at Bio-Rad CFX96 Thermocycler. All primers used in this manuscript are listed in the Supplementary Table 1.

**Miles Assay**

Miles Assay is undertaken accordingly as noted in Diana Moughon et al [2](#_ENREF_2)

**Promoter reporter assay**

The validation of interaction of HIF1A and POSTN promoter was undertaken by the manual of Promega vectors pGL3-basic and pRL-TK. The vectors were cloned as described in the section of “Cells, plasmids and Reagents” and 293 cells were seed in a 24-well plate at 1x10^5/well on day 0. Then the pGL3-basic and pRL-TK plasmids were transfected into all wells, with HIF1A overexpressing plasmid in experimental group and its control plasmids in control group were transfected with FuGENE HD transfection agent (Cat#E2311, Promega). Upon 48 hours incubation, cells were lysed and measured by CLARIOstar Plus plate reader (BMG Labtech, USA).

**Time-lapse microscopy for 2D scratch assay and 3D migration assay**

A total of 1x10^5 tumor cells (e.g., 5x10^4 cells each of VHL-WT and VHL-KO cells) were grown on a 24-well plate until reaching 90% confluence. The bottom of each well was scratched with the end of a 200 µl tip to form a gap. The cell migration was monitored continuously with a Nikon Eclipse Ti-E time-lapse microscope using a 10X objective, and a humidified, 37 °C environment containing 5% CO2. Specific fields of interest were set and recorded at 15 minute intervals for 20 hours using the FITC and TRITC channels. Nikon elements software was used to measure the migration speed of cells in each group.

Transwell chambers (0.4 μm pore size, Thermo Fisher, catalog number: CLS3470-48EA) were assembled in a 24-well plate. One milliliter of RPMI-1640 medium supplemented with 10% fetal bovine serum and 50 ng/mL EGF was added to the bottom chamber. HUVECs were seeded on the bottom of the Transwell chamber at a cell number of 1x10^5. On day 2, a layer of Matrigel (Corning, catalog number: 356234) was coated on top of the layer of HUVECs and placed back in a 37 °C incubator to solidify: 100 µL for migration assay or 30 µL for 3D in vitro intravasation assay. Tumor cells (1x10^5) were then seeded onto the top of the Matrigel. A Nikon Eclipse Ti-E time-lapse confocal microscope was used to image cell migration. The z-step parameters were set with the HUVEC cell layer as the bottom and the tumor cell layer as the top with approximately 200 stepwise stacks for scanning every 15 minutes for 48 hours.

**Western blot, necroptosis, and apoptosis reporter assay**

For Western blot, 1x10^6 HUVECs were seeded onto the bottom of 6-well-plate Transwell chambers (1 μm pore size, Falcon, catalog number: 353102) with 1x10^6 tumor cells in the top chamber, with or without 1 μg/mL anti-POSTN MPC5B4 monoclonal antibody (mAb), with or without cilengitide in concentrations indicated in the figure legends. Cells were harvested after 48 hours for whole-cell-lysate protein extraction with RIPA buffer (ThermoFisher, catalog number: 89901) supplemented with proteinase inhibitors (Thermo Fisher, catalog number: 78430). Samples were then boiled for 10 minutes in 6X SDS loading buffer and loaded onto the 10% gels. Blots were probed with anti-phospho-RIP (Ser166)(1:1000), anti-RIP(1:1000), anti-phospho-MLKL (Ser358)(1:1000), anti-MLKL(1:1000), anti-caspase-3(1:1000), and anti-cleaved caspase-3(1:1000)from the Apoptosis/Necroptosis Antibody Sampler Kit (Cell Signaling Technology, MA, USA, catalog number: 92570). Blots were imaged and analyzed on a ChemiDoc XRS+ with associated Image Lab software (Bio-Rad).

For the necroptosis reporter assay, 24-well-plate Transwell chambers (0.4 μm pore size, Thermo Fisher, CA, USA, catalog number: CLS3470-48EA) were seeded with 1x10^5 HUVECs on the bottom and 1x10^5 tumor cells on the top of the chamber with or without 1µg/mL anti-POSTN MPC5B4 mAb. After 48 hours, HUVECs were washed with PBS once and a solution of 1.6 μM ethidium homodimer III (EthD-III, Biotium, CA, USA, catalog number: 400050) and 2 μM Hoechst33342 (Biotium, CA, USA, catalog number: 40045) were added to cells and incubated in a humidified, 5% CO2 incubator at 37 °C for 15 minutes. Microscope images were taken of five random fields of each well with a 10X objective in DAPI and TRITC channels and quantified with ImageJ.

For apoptosis evaluation, HUVECs were cultured in Transwell chambers as described above. After 48 hours, the plates were equilibrated at room temperature for 10 minutes, and 200 μL of Caspase-Glo 3/7 reagent (Promega, catalog number: G8090) was added to each well. After being placed on a shaker at 300-500 RPM for 30 seconds, the reaction was incubated at room temperature for 1 hour and then analyzed for luminescence with a Synergy HT microplate reader (BioTek).

**Cell proliferation assay**

Cell proliferation was measured using the MTS assay and direct cell counting. For both assays, cells in log phase were counted and seeded on day 0 at a density of 1000 cells per well onto a 96-well plate, or 500 cells per well onto a 384-well plate. For the MTS assay, cell numbers were evaluated every 24 hours on days 1, 2, 3, 4, 5, and 6 using the MTS kit (Promega, CA, USA, catalog number: G3582) and measured with a Multiskan MK3 microplate reader (Thermo, USA). For direct cell counting, an ImageXpress workstation was used to photograph each well of a 384-well plate and count the DAPI-stained cells.

**Flow cytometry**

Primary tumors and lungs of mice were dissected, minced into small pieces, and digested with 0.2% collagenous II at 37 °C on a 100 RPM shaker. The cell suspensions were passed through 70-µm cell strainers. The digested cells were stained with Hoechst 33342 for 15 minutes and analyzed by flow cytometry. Similarly, chicken and mouse blood were collected and lysed with red blood cell lysis buffer (BD Bioscience, USA, catalog number: 555899). Cells were then analyzed by flow cytometry for mStrawberry and EGFP expression.

**Isolation and cultivation of primary ccRCC tumor cells.**

With the consent of patients, primary ccRCC tumor samples were collected and chopped into pieces with sterile scissors and scalpels into RPMI-1640. Tissue chunks were transferred to a 15-mL conical tube and centrifuged at 300 x g at room temperature for 5 minutes. The supernatants were carefully discarded and the tissue pellet was resuspended in 2.6-mL prediluted 3 U/L Liberase TM (Sigma-Aldrich, catalog number: 5401119001) in RPMI-1640 media. The tube was placed on a100 RPM rotator at 37 °C for 1 hour. When the tissue was fully digested and no chunks were visible, cells were centrifuged at 300 x g at room temperature for 5 minutes. The pellet was further treated with prediluted 1X red blood cell lysis buffer (BD Biosciences, catalog number: 555899) in sterile water for 15 minutes and washed once with PBS. Cells were resuspended in RPMI-1640 supplemented with 10% fetal bovine serum and 1X penicillin/streptomycin and cultured in a humidified, 5% CO2 incubator at 37 °C.

**VHL stability test**

786-O cells were cultured and seeded in the 6-well plate at 5x10^5 cells per well on day 0. On day 1, each well was transfected with either 3000ng wildtype VHL or L169P variant plasmid with 9ul Promega FuGENE transfection reagent (cat# E2311, Promega, USA) followed with 24 hours incubation. Upon harvest, cycloheximide (CHX, 100μg/ml, Cat# 357420010, Acros Organics, USA) was added on each well and RIPA lysis buffer was used to harvest cells at 0, 3 and 6 hours upon CHX addition. The harvested protein was subjected to western blot analysis as mentioned earlier.

**Human ccRCC patient specimens**

The tissue microarray was constructed from a cohort of 357 patients who underwent nephrectomy for sporadic RCC at UCLA between 1989 and 2000, as previously described [3](#_ENREF_3). Clinical data, including age, gender, Eastern Cooperative Oncology Group performance status, and pathologic data (including tumor-node-metastasis stage, histologic subtype, and Fuhrman grade) were collected for each case. This study was approved by the UCLA Institutional Review Board.

Large tumor tissues from primary tumors, locally invasive tumors, or metastases were obtained from 26 patients who underwent radical nephrectomy in the Department of Urology at the Ronald Regan Medical Center, UCLA, from 2015 to 2018. All patients provided informed consent before surgery, and all experiments were performed according to the approved guidelines, complying with the principles for the use of human tissues under the Declaration of Helsinki. This study was approved by the Institutional Review Board of UCLA, IRB Protocol #11-001363.

**Supplementary table 1: Primer sequences**

|  |  |  |
| --- | --- | --- |
| Primer Name | strand | Sequence (5'-3') |
| Human-E-cadherin | forward | CGAGAGCTACACGTTCACGG |
| reverse | GGGTGTCGAGGGAAAAATAGG |
| Human-N-Cadherin | forward | TCAGGCGTCTGTAGAGGCTT |
| reverse | ATGCACATCCTTCGATAAGACTG |
| Human-MMP9 | forward | TGTACCGCTATGGTTACACTCG |
| reverse | GGCAGGGACAGTTGCTTCT |
| Human-HIF1A | Forward | ATCCATGTGACCATGAGGAAATG |
| Reverse | TCGGCTAGTTAGGGTACACTTC |
| Human-HIF2A | Forward | TTGCTCTGAAAACGAGTCCGA |
| Reverse | GGTCACCACGGCAATGAAAC |
| Mouse-E-cadherin | forward | CAGGTCTCCTCATGGCTTTGC |
| reverse | CTTCCGAAAAGAAGGCTGTCC |
| Mouse-N-Cadherin | forward | AGCGCAGTCTTACCGAAGG |
| reverse | TCGCTGCTTTCATACTGAACTTT |
| Mouse-MMP9 | forward | CTGGACAGCCAGACACTAAAG |
| reverse | CTCGCGGCAAGTCTTCAGAG |
| Mouse-alpha-SMA | forward | GTCCCAGACATCAGGGAGTAA |
| reverse | TCGGATACTTCAGCGTCAGGA |
| Mouse Periostin | Forward | CACGGCATGGTTATTCCTTCA |
| reverse | TCAGGACACGGTCAATGACAT |

**Supplementary table 2: Heatmap gene list** (not in the same order as shown in Figure 2I)

|  |  |  |  |
| --- | --- | --- | --- |
|  | scRNAseq | RENCA | ACHN |
| LTN1 | 0.029949671 | 0.216259635 | -0.244046986 |
| SPRY2 | -0.004380649 | 0.459421787 | 0.802698714 |
| USP16 | -0.000114495 | 0.235033035 | 0.000230538 |
| TSC22D1 | -0.025668863 | 0.54509172 | -0.41371657 |
| LHFPL6 | -0.017287333 | 1.340616172 | -0.003494214 |
| APP | 0.020125674 | 0.453180406 | -0.091447121 |
| LACC1 | -0.017968804 | 0.296739654 | 0 |
| SCAF4 | -0.067969505 | 0.21401484 | 0.159967507 |
| GATD3B | 0.007226167 | -0.177075597 | -0.154909609 |
| PI4KA | 0.012392537 | 0.047625758 | -0.362028499 |
| PHF11 | -0.036077527 | 0.016611075 | 0 |
| CRYL1 | 0.102073523 | -0.175206023 | -1.372718193 |
| ELF1 | 0.01428615 | 0.193623564 | -0.351503747 |
| TGDS | -0.031250404 | 0.240657204 | -0.719228493 |
| PSMG2 | 0.018758002 | 0.132350191 | 0 |
| PSPC1 | 0.006439259 | 0.153276785 | 0.071533313 |
| NDUFV2 | 0.011319559 | -0.063061321 | -0.066775978 |
| GTF3A | 0.005442852 | 0.301256151 | 0.240531924 |
| DNAJC15 | 0.006295613 | -0.04245555 | 0 |
| CAB39L | 0.006307857 | -0.921437957 | -0.549919512 |
| MPHOSPH8 | 0.008606336 | -0.105851842 | 0.307111528 |
| FHOD3 | 0.086128862 | -0.126003949 | -0.253258758 |
| IL17RA | -0.003194394 | 0.149905586 | -0.366139862 |
| KATNAL1 | -0.045523327 | 0.064094925 | 0.656973322 |
| CHMP1B | 0.012205839 | -0.241737868 | 0.038834937 |
| KPNA3 | -0.034370674 | 0.383123218 | 0.341337115 |
| TMEM50B | -0.042203235 | -0.938410916 | 1.293829406 |
| B3GLCT | -0.002101911 | -0.108875852 | 0 |
| PAN3 | -0.02087726 | -0.111313071 | 0.411993587 |
| METTL4 | -0.036433048 | 0.024693983 | 0 |
| GART | 0.019316566 | 0.414009023 | -0.334226397 |
| THOC1 | -0.091948675 | 0.126644198 | 0.224440511 |
| CCT8 | 0.021592092 | 0.371413436 | 0.014382988 |
| SAP18 | 0.038138622 | 0.703984565 | 0.19489591 |
| TBC1D4 | -0.037566604 | 0.533558478 | -0.285812074 |
| USP14 | 0.038433147 | 0.380810136 | 0.112531799 |
| UFM1 | 0.014382199 | -0.118102997 | 1.141193957 |
| CCDC122 | -0.01402147 | 0.066287014 | -0.107584259 |
| PIK3C3 | 0.023648788 | -0.071157384 | 0.968983566 |
| PROSER1 | -0.045532276 | 0.182970939 | 0 |
| DONSON | -0.053238758 | -0.057225447 | -0.614444565 |
| RAB31 | 0.043382136 | -0.337296545 | -0.564208472 |
| SKA3 | -0.079767763 | 0.253112291 | 1.726455568 |
| MIPEP | 0.001046048 | 0.009989601 | 0.159097062 |
| GTF2F2 | -0.008380017 | 0.223072236 | -0.363829322 |
| RWDD2B | -0.015866189 | 0.05090644 | 0.570753568 |
| MED15 | -0.026637747 | 0.248915471 | 0.490193338 |
| MAPRE2 | -0.020010785 | -0.373551137 | -0.034813529 |
| PIBF1 | -0.01490406 | 0.118917244 | 0.175726102 |
| KLF5 | -0.021061328 | 1.830117243 | -0.222424082 |
| URB1 | -0.001845171 | 0.338767946 | 0.977628348 |
| FNDC3A | 0.034920668 | -0.008311107 | 0.053670049 |
| SETDB2 | -0.013869473 | 0.175070266 | -0.096796598 |
| YES1 | -0.065163816 | -0.080281182 | -0.129600015 |
| SLC5A3 | -0.026163414 | -2.232188386 | -0.349568779 |
| CHAF1B | -0.000817915 | -0.070582393 | 0.295882386 |
| MRPS6 | 0.023990202 | -1.735474351 | 0 |
| MPPE1 | 0.020551726 | -1.236698169 | 0 |
| OSBPL1A | -0.029964436 | -0.44073452 | 0.671476588 |
| HMGB1 | -0.302285567 | 0.244773558 | 0.09192867 |
| MZT1 | -0.088049752 | 0.631891994 | 0.095648525 |
| MRPL57 | 0.054301504 | 0.091382351 | 0 |
| SLC25A15 | 0.000934026 | -0.201261873 | -0.0559697 |
| IMPA2 | 0.114518842 | 0.387779653 | -1.354578711 |
| PARP4 | 0.035222289 | -0.012456644 | -0.590246179 |
| CXADR | -0.033936551 | 2.018312006 | 0 |
| HSPH1 | -0.118640371 | -0.017372665 | 0.136204702 |
| NDC80 | -0.085217579 | -0.213932782 | -0.190186725 |
| LNX2 | -0.006647531 | 0.143269871 | 1.687354294 |
| NUFIP1 | 0.032260082 | 0.900531899 | -0.014557074 |
| USPL1 | 0.003028246 | 0.409316793 | -0.745908307 |
| POMP | -0.056626815 | 0.063782558 | -0.257457034 |
| MTCL1 | 0.069080427 | 0.040189104 | -0.006771509 |
| OPTN | 0.058246493 | -0.286353213 | 0.314241192 |
| ATP9A | 0.030520607 | -0.382499106 | -0.360694172 |
| IFT27 | 0.01593635 | -0.200273005 | 0 |
| PISD | 0.035302873 | 0.202793403 | 0.086844983 |
| DYNLT3 | -0.010301747 | 0.104507568 | 0.105123037 |
| TTLL12 | 0.000606516 | 0.494949508 | -0.129384807 |
| PTGIS | 0.04413237 | 1.286564677 | -1.323248724 |
| STK11 | 0.000837313 | -0.06489724 | 0.414331162 |
| ATP9B | -0.004919215 | -0.408479404 | -1.536532809 |
| RNF114 | 0.030950793 | -0.055121537 | -0.101298783 |
| STARD13 | -0.012802636 | 0.151978771 | -0.691067961 |
| DSTN | -0.032200994 | 1.334089192 | 0.389005549 |
| POLRMT | -0.03459413 | -0.070900741 | 0.288465817 |
| SKA1 | -0.030812004 | 0.087538865 | 0 |
| AK3 | 0.011581844 | -0.594495471 | 0.393571862 |
| POLR1D | 0.019320043 | 0.298258553 | -0.235655755 |
| TXN2 | 0.032061323 | 0.060051749 | 0 |
| SLC39A6 | 0.028440924 | 0.072617286 | 0.393960356 |
| ETS2 | -0.038523198 | 0.628839114 | -0.546124846 |
| MAP1LC3A | 0.026276283 | -0.787277806 | -2.135865669 |
| EIF3D | 0.071123433 | 0.19224557 | 0.300966782 |
| SEPHS1 | -0.049493719 | -0.004831018 | -0.419477032 |
| PSTPIP2 | -0.010071475 | -0.227368408 | -1.511074527 |
| WDR13 | 0.02497332 | -0.415008232 | 0.427170804 |
| IPO5 | -0.052246651 | 0.870116625 | 0.048368778 |
| PSMG3 | -0.038182534 | 0.170877263 | -0.170889936 |
| TUBGCP3 | -0.018170643 | -0.010185271 | -0.274447085 |
| ZYX | 0.061664646 | 0.391704367 | 0.245784731 |
| NSF | 0.005868079 | 0.028397755 | 0.040950567 |
| PLXNB2 | 0.095441947 | 0.351964923 | 0.137083775 |
| CHD1 | 0.039036447 | 0.294164248 | 0.294818565 |
| LRRFIP2 | 0.014007181 | 0.074008514 | 0.09999971 |
| EIF4E2 | 0.039815244 | 0.197870123 | 0.102019734 |
| SIDT2 | 0.019061135 | 0.050377129 | 0.014322314 |
| SPOP | 0.048758886 | 0.032339381 | 0.121040421 |
| MEA1 | 0.05498862 | 0.113308498 | 0.240451561 |
| DDB1 | 0.036691685 | 0.262748754 | 0.213653803 |
| LIAS | 0.003125193 | 0.020250712 | 0.022734705 |
| SGMS2 | 0.037401766 | 0.229023413 | 0.268105505 |
| WAC | 0.047529237 | 0.291516643 | 0.192524675 |
| GTF2F1 | 0.043209905 | 0.304243911 | 0.285369277 |
| MELTF | 0.062156212 | 0.075092078 | 0.010871311 |
| ELAVL1 | 0.044303355 | 0.171200722 | 0.260656631 |
| MITF | 0.093987613 | 0.070608557 | 0.241661302 |
| PHAX | 0.02409906 | 0.150337049 | 0.164059907 |
| ABCF1 | 0.041824951 | 0.269207719 | 0.275590927 |
| SRA1 | 0.057506695 | 0.247136151 | 0.349428284 |
| DLG5 | 0.016372379 | 0.105817992 | 0.089408936 |
| MAPRE1 | 0.066312384 | 0.029376189 | 0.017623718 |
| CWC15 | 0.049734096 | 0.052263104 | 0.14781658 |
| VEGFA | 0.067477297 | 0.381506867 | 0.42800118 |
| CEBPZ | 0.054341186 | 0.335826356 | 0.322287243 |
| CTNND1 | 0.063080571 | 0.23188091 | 0.102248541 |
| PRKCA | 0.032699701 | 0.161905441 | 0.096375354 |
| RNF7 | 0.046409826 | 0.007763954 | 0.045514976 |
| GRHPR | 0.182021928 | 0.873533652 | 0.512538935 |
| ZNF451 | 0.028741342 | 0.137562267 | 0.170423932 |
| UBXN1 | 0.083457635 | 0.265186675 | 0.104640836 |
| QTRT1 | 0.035486474 | 0.18310564 | 0.206625055 |
| YTHDC1 | 0.037157295 | 0.179649726 | 0.215160565 |
| FAM53C | 0.030435855 | 0.169505611 | 0.129422907 |
| FOXP4 | 0.024907792 | 0.075200864 | 0.120192131 |
| FAM168A | 0.020631603 | 0.049773332 | 0.01539255 |
| BICD2 | 0.056518981 | 0.280995504 | 0.188596153 |
| CHMP2A | 0.071290475 | 0.013636599 | 0.052265177 |
| SLC6A8 | 0.076826585 | 0.022995846 | 0.034017516 |
| KIAA0100 | 0.024849426 | 0.131478747 | 0.115821976 |
| NOP53 | 0.188120185 | 0.678050069 | 0.327649165 |
| MMUT | 0.01151153 | 0.060533491 | 0.052965193 |
| RTCB | 0.034768872 | 0.126102195 | 0.172455892 |
| RNMT | 0.043763414 | 0.16067524 | 0.217422187 |
| LSM14A | 0.029632884 | 0.141082028 | 0.097459538 |
| ZFR | 0.032353834 | 0.14825829 | 0.16589233 |
| EIF3E | 0.087972002 | 0.189681943 | 0.346779061 |
| LCOR | 0.028355703 | 0.136193579 | 0.102804615 |
| TIPARP | 0.046876458 | 0.229477434 | 0.187039825 |
| RNF25 | 0.036801002 | 0.105022079 | 0.042153524 |
| PEA15 | 0.076063819 | 0.25384946 | 0.353530737 |
| EIF3D | 0.071123433 | 0.19224557 | 0.300966782 |
| SGF29 | 0.036884819 | 0.079504742 | 0.025197034 |
| CUL3 | 0.032338299 | 0.035917939 | 0.088430796 |
| UBE2Z | 0.072975404 | 0.32790456 | 0.272318335 |
| TCF25 | 0.066245006 | 0.264367131 | 0.288911709 |
| SPIN1 | 0.046342078 | 0.193753197 | 0.195023869 |
| BMP1 | 0.047506301 | 0.121980115 | 0.185223497 |
| ARL3 | 0.048170409 | 0.181844799 | 0.200028075 |
| FNDC3B | 0.051091151 | 0.06252387 | 0.141106478 |
| PBX2 | 0.030690962 | 0.119354763 | 0.124807376 |
| MCFD2 | 0.054724283 | 0.149325671 | 0.212897167 |
| CTDNEP1 | 0.048709141 | 0.155010295 | 0.083191701 |
| ZNHIT1 | 0.093977074 | 0.365270317 | 0.33859492 |
| AP3S1 | 0.071586615 | 0.035127308 | 0.118492463 |
| DDX56 | 0.084614638 | 0.314518089 | 0.233251445 |
| RBM42 | 0.028092162 | 0.038728363 | 0.07839812 |
| ELOB | 0.087350588 | 0.089744889 | 0.210956157 |
| DCUN1D3 | 0.062547767 | 0.226162975 | 0.21505998 |
| RAI14 | 0.078718376 | 0.151306868 | 0.052611436 |
| SF3B2 | 0.035837957 | 0.130626631 | 0.10765477 |
| FRA10AC1 | 0.01310695 | 0.017008753 | 0.004811964 |
| MRPL32 | 0.059571676 | 0.131380566 | 0.055328524 |
| TAF12 | 0.044857257 | 0.025270012 | 0.075305165 |
| TOPORS | 0.035122195 | 0.027249181 | 0.010533879 |
| TIMM9 | 0.075395647 | 0.169022097 | 0.239823293 |
| UBE3B | 0.04056258 | 0.100712553 | 0.051117955 |
| CCDC80 | 0.081317772 | 0.239713027 | 0.248267945 |
| PAIP1 | 0.051585503 | 0.110078185 | 0.153910641 |
| RAB18 | 0.052932915 | 0.095047031 | 0.147604042 |
| LASP1 | 0.050356937 | 0.08102761 | 0.13250203 |
| MAGED1 | 0.067617595 | 0.174843037 | 0.105170605 |
| PSMB5 | 0.097398537 | 0.187739348 | 0.086962362 |
| GLIS3 | 0.077883544 | 0.100919912 | 0.175517723 |
| EHMT1 | 0.020652862 | 0.051953147 | 0.036512383 |
| PSMC1 | 0.045322427 | 0.107758381 | 0.112950193 |
| TRIAP1 | 0.054019576 | 0.066333201 | 0.117375465 |
| CIAO1 | 0.057523479 | 0.027515009 | 0.06966866 |
| EIF3H | 0.097278737 | 0.23675541 | 0.189348184 |
| PSMB4 | 0.069200873 | 0.113932044 | 0.159279194 |
| NUTF2 | 0.059853882 | 0.132772729 | 0.13577629 |
| BTF3 | 0.047689249 | 0.058799547 | 0.097668286 |
| PITPNB | 0.038212874 | 0.054338099 | 0.080562757 |
| NMT1 | 0.05355703 | 0.061573568 | 0.029671073 |
| NCOA4 | 0.085565125 | 0.17025605 | 0.156753226 |
| RPRD2 | 0.086748757 | 0.049587284 | 0.088567295 |
| RPF2 | 0.072007906 | 0.057843848 | 0.101713535 |
| CAV2 | 0.110731122 | 0.183301521 | 0.167618168 |
| JUND | 0.141582858 | 0.176186811 | 0.205387289 |
| PPP4R3B | 0.043474107 | 0.052805942 | 0.049071585 |

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