# Supplementary Materials: RKIP Regulates Differentiation-Related Features in Melanocytic Cells

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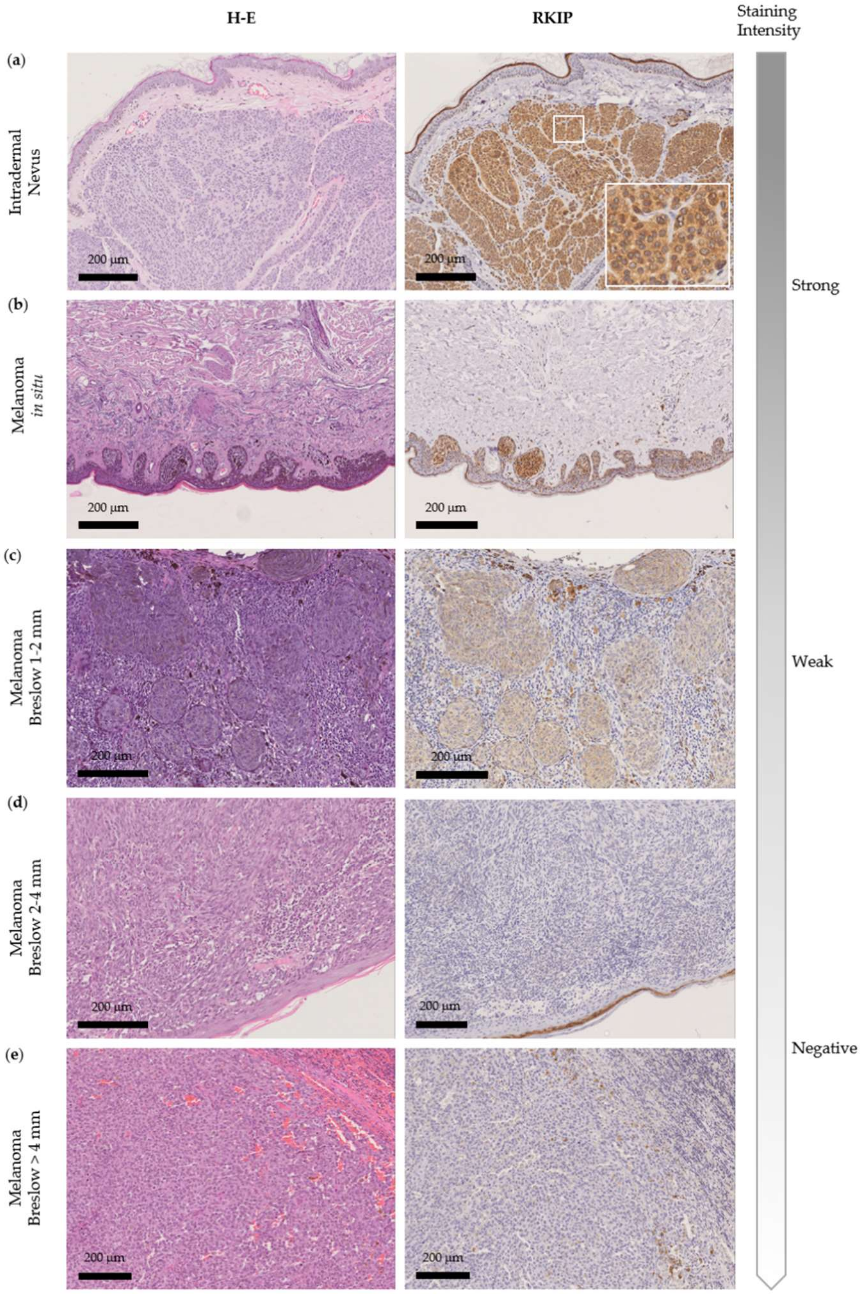

**Figure S1.** Representative images of manually scored RKIP staining categories in FFPE biopsies from patients. At the feft: Hematoxylin-Eosin staining (H-E). At the right: Immunohistochemistry (IHC) of RKIP for increasing Breslow Index. (**a**-**b**) Strong staining for intradermal nevus and in situ melanoma, respectively; (**c**) weak staining for a melanoma with Breslow Index between 1 and 2 mm; (**d**-**e**) negative staining for melanomas thicker than 2 mm.

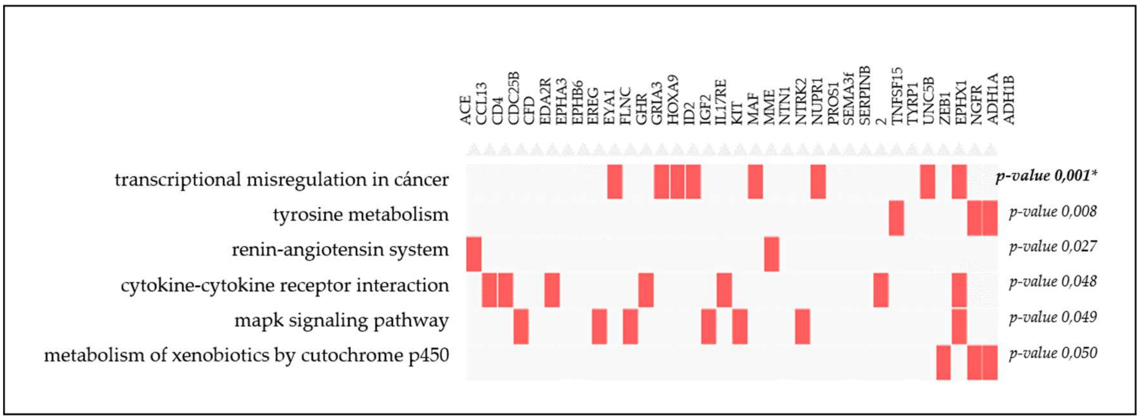

**Figure S2.** RNA Sequencing data analysis. Each row of the figure represents an over-represented gene signature generated by analyzing the up-regulated and down-regulated genes from a differential expression analysis of RKIP Knockdown melanocytes HEMn-LP. Results from the EnrichR Website with a *p*-value > 0.05.

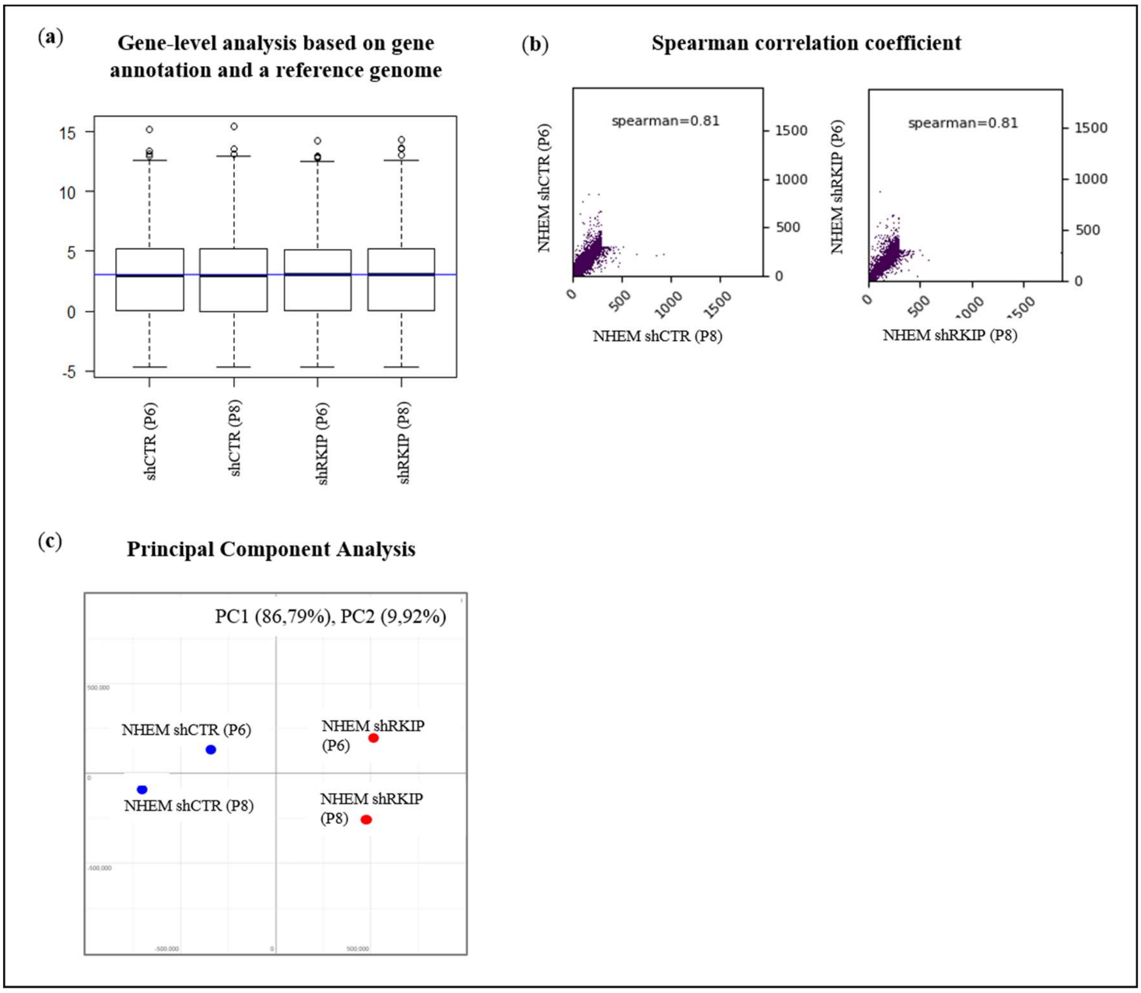

**Figure S3.** RNA Sequencing data quality. (**a**) Read counts normalization per sample; (**b**) Spearman correlation coefficient between replicates; (**c**) Principal component analysis for replicates.

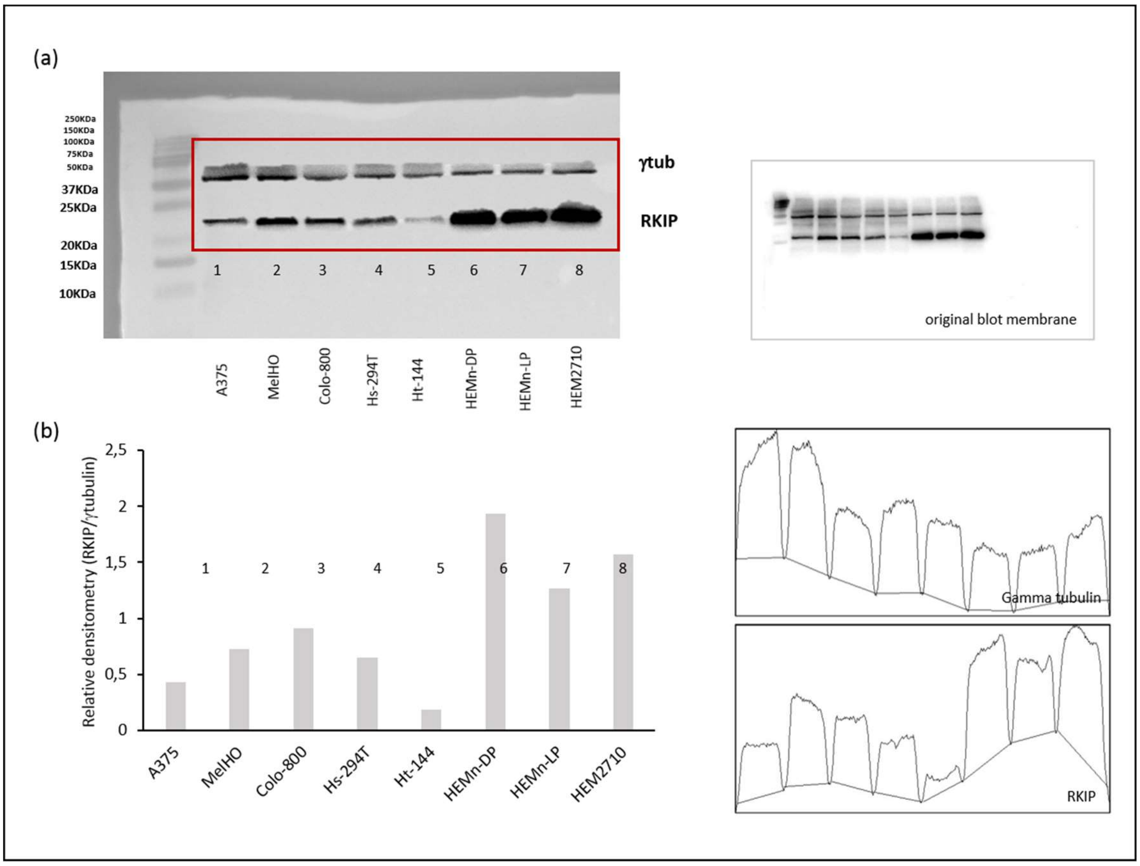

**Figure S4.** Details of Western Blot from Figure 2 related with RKIP expression in several cell lines. (**a**) Blots for RKIP and γTubulin in primary and metastatic melanoma and in three primary melanocytes HEMn-DP (dark pigmented), HEMn-LP (light pigmented) and HEM2710. On the right, original blot for each analyzed protein. Highlighted with a red square the information included in the Figure 3 (horizontal rotation). (**b**) Densitometry from the plots showing the relative level of RKIP/γtubulin. On the right, the peak plots for each protein analyzed (γTubulin and RKIP, respectively).

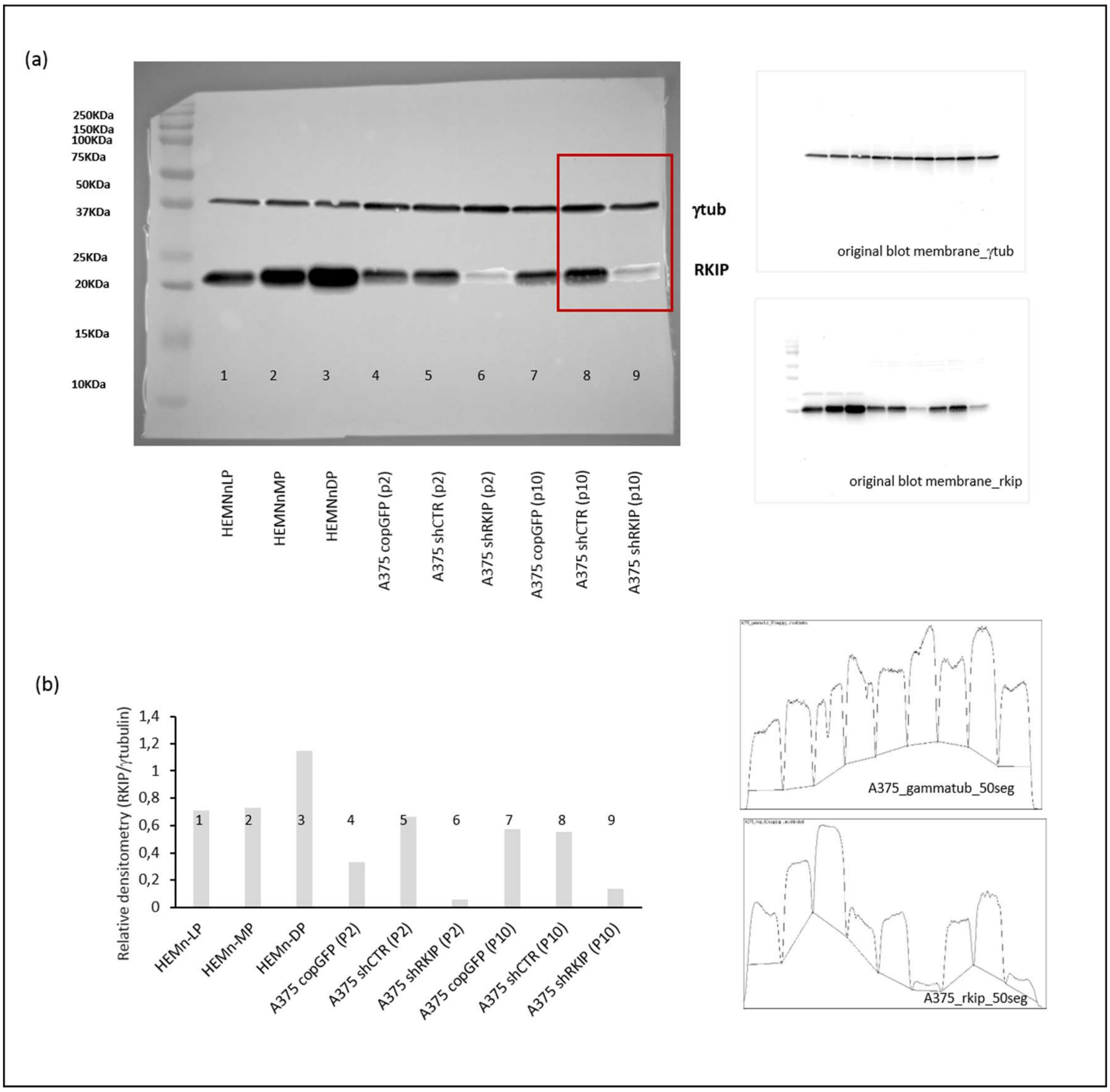

**Figure S5.** Details of Western Blot from Figure 3 related to information of A375 melanoma cell line. (**a**) Blots for RKIP and γTubulin in three primary melanocytes HEMn-LP (light pigmented), HEMn-MP (medium pigmented) and HEMn-DP (dark pigmented) and in A375 melanoma cells (two consecutive passages after transfection for down regulation of endogenous RKIP). On the right, original blots for each analyzed protein. Information included in the Figure 3 has been highlighted with a red square. (**b**) Densitometry from the plots showing the relative level of RKIP/γtubulin. On the right, the peak plots for each analyzed protein (γTubulin and RKIP, respectively).

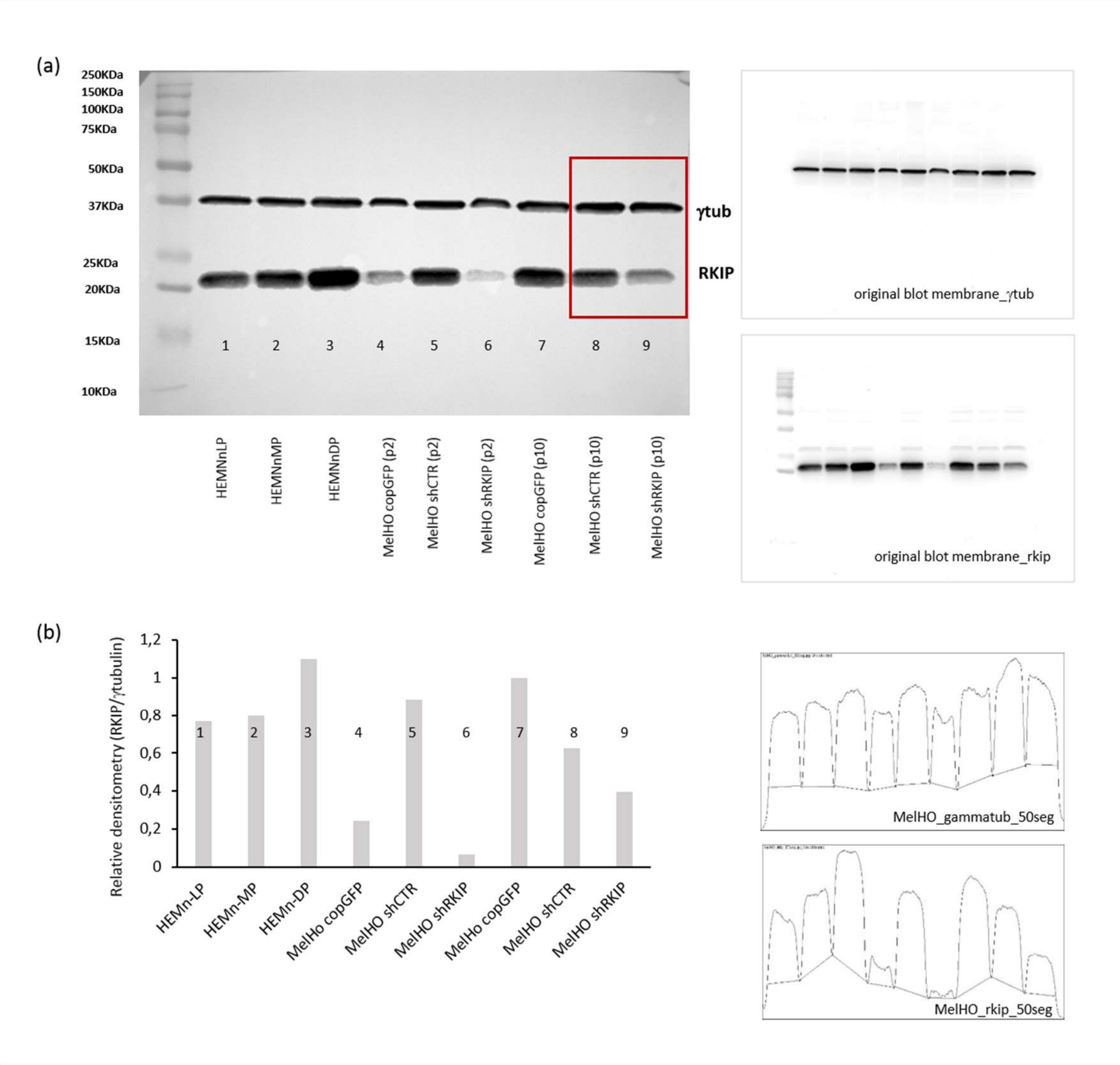

**Figure S6.** Details of Western Blot from Figure 3 related to information of MelHO melanoma cell line. (**a**) Blots for RKIP and γTubulin in three primary melanocytes HEMn-LP (light pigmented), HEMn-MP (medium pigmented) and HEMn-DP (dark pigmented) and in MelHO melanoma cells (two consecutive passages after transfection for RKIP down regulation). On the right, original blots for each analyzed protein. Highlighted with red square the information included in the Figure 3. (**b**) Densitometry from the plots showing the relative level of RKIP/γtubulin. On the right, the peak plots for each protein analyzed (γTubulin and RKIP, respectively).

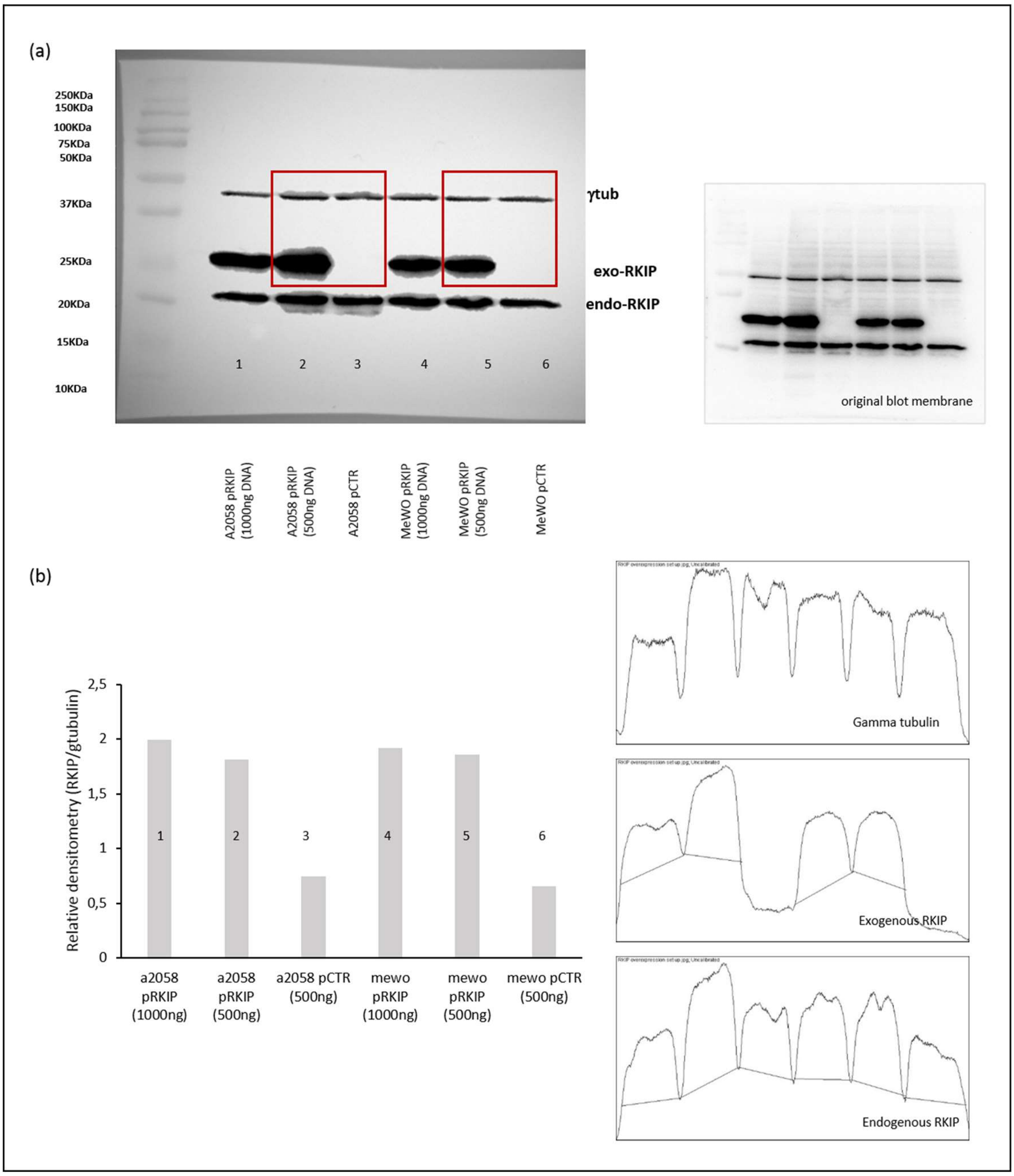

**Figure S7.** Details of Western Blot from Figure 4 related to the information regarding MeWO and A2058 melanoma cell lines. (**a**) Blots for RKIP (1000 ng and 500 ng of plasmid for overexpression of RKIP) and γTubulin. RKIP plasmid (Myc-DDK-tagged) encodes for a RKIP protein 4KDa bigger than the endogenous RKIP. Therefore, blots belonging to transfected samples contain 2 lines (endogenous and overexpressed forms of RKIP). On the right, the original blot. Red squares highlight the blot fraction employed for the Figure 5 (horizontal rotation). (**b**) Densitometry from the plots showing the relative level of RKIP/γtubulin. In this case, the values of endogenous and exogenous RKIP have been added to calculate relative expression. On the right, the peak plots for each analyzed protein (γTubulin, exogenous RKIP and endogenous one, respectively).

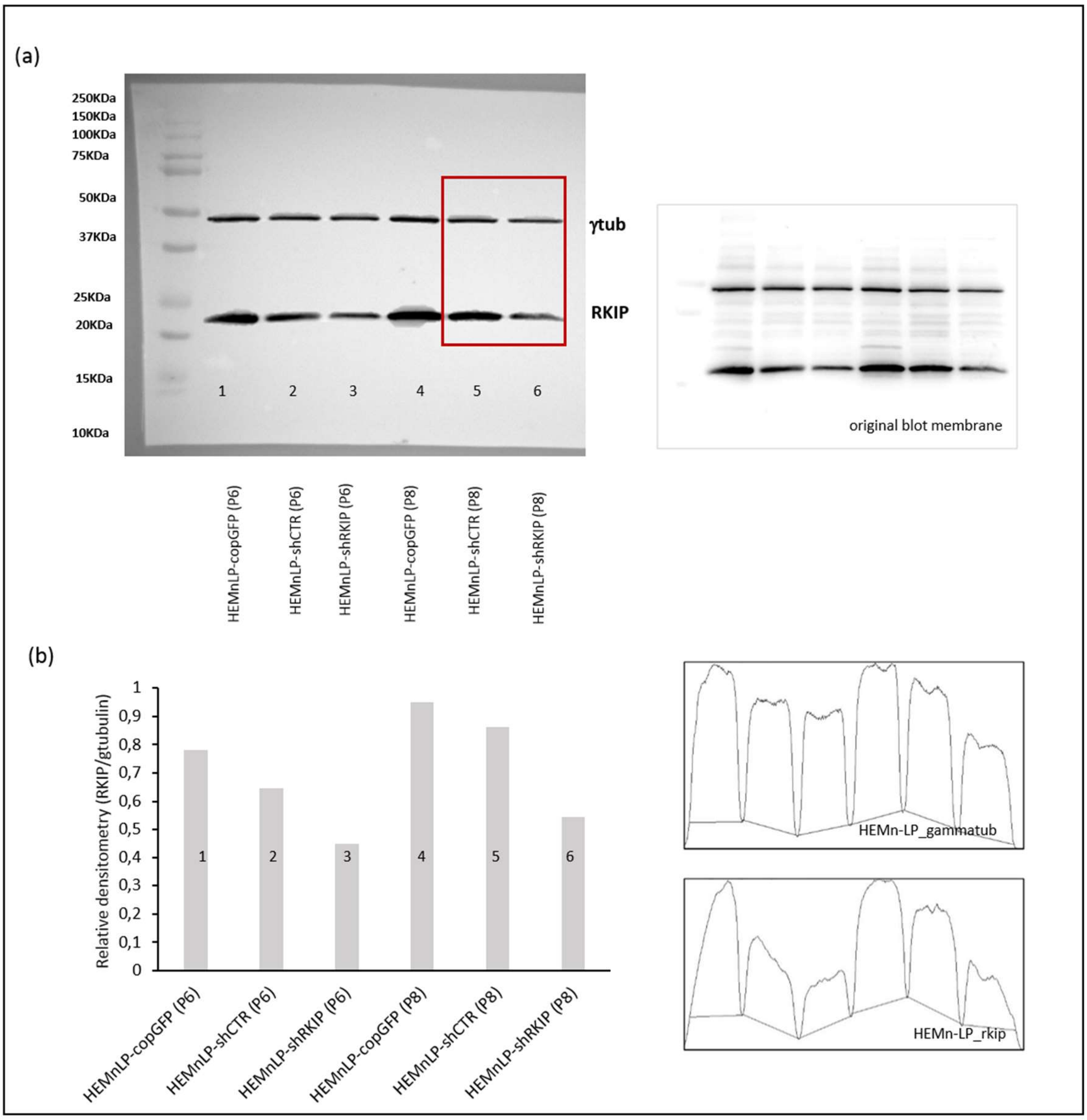

**Figure S8.** Details of Western Blot from Figure 5 related to primary melanocytes (HEMn-LP). (**a**) Blots for RKIP and γTubulin in two consecutive passages of primary melanocytes HEMn-LP after transfection with lentiviral particles in order to down regulate endogenous RKIP. On the right, original blot for both analyzed proteins. Highlighted with red square the information included in the Figure 5. (**b**) Densitometry from the plots showing the relative level of RKIP/γtubulin. On the right, the peak plots for each analyzed protein (γTubulin and RKIP, respectively).

**Table S1.** Differentially expressed genes after RKIP silencing. The details of Log Fold Change, P-Value and False Discovery Rate are specified in each column.

| **Gene Symbol** | **logFC** | ***p*-Value** | **FDR** |
|---|---|---|---|
| AC008105.3 | −1.935 | 0.001 | 0.049 |
| AC025125.1 | −3.192 | 0.000 | 0.006 |
| AC025594.1 | −2.906 | 0.000 | 0.024 |
| AC079949.2 | −5.287 | 0.000 | 0.015 |
| AC115090.1 | 5.285 | 0.000 | 0.013 |
| AC244153.1 | 5.285 | 0.000 | 0.013 |
| ACE | −2.512 | 0.001 | 0.048 |
| ADAMTS12 | 1.076 | 0.000 | 0.031 |
| ADAMTS15 | 2.391 | 0.000 | 0.032 |
| ADAP1 | −1.024 | 0.000 | 0.041 |
| ADD3 | −1.340 | 0.001 | 0.048 |
| ADH1A | 2.779 | 0.000 | 0.006 |
| ADH1B | 2.784 | 0.000 | 0.014 |
| AL359258.1 | −2.534 | 0.000 | 0.038 |
| AL390038.1 | −2.551 | 0.000 | 0.038 |
| AL512329.2 | 4.490 | 0.000 | 0.036 |
| ALPL | 1.145 | 0.000 | 0.041 |
| ANLN | 0.857 | 0.000 | 0.046 |
| APOL1 | −4.465 | 0.000 | 0.006 |
| ARHGAP26 | −1.144 | 0.000 | 0.038 |
| ARHGEF28 | −1.141 | 0.000 | 0.038 |
| ARHGEF6 | −1.208 | 0.000 | 0.027 |
| ATP10A | −2.236 | 0.000 | 0.031 |
| AURKC | −3.040 | 0.000 | 0.022 |
| BCL3 | 1.156 | 0.000 | 0.024 |
| BST2 | −1.184 | 0.001 | 0.049 |
| C1orf216 | −1.123 | 0.000 | 0.033 |
| C1orf54 | −3.151 | 0.000 | 0.040 |
| C1QTNF7 | −3.849 | 0.000 | 0.038 |
| C21orf91−OT1 | −1.106 | 0.000 | 0.041 |
| C2CD6 | 2.086 | 0.000 | 0.028 |
| C8orf31 | 1.990 | 0.000 | 0.037 |
| CAPG | 2.620 | 0.000 | 0.022 |
| CCDC3 | 2.572 | 0.000 | 0.041 |
| CCL13 | 1.650 | 0.001 | 0.048 |
| CD302 | 1.620 | 0.000 | 0.023 |
| CD4 | −5.673 | 0.000 | 0.017 |
| CDC25B | 1.247 | 0.000 | 0.038 |
| CDK18 | 2.649 | 0.000 | 0.013 |
| CDO1 | 2.221 | 0.000 | 0.024 |
| CDON | 1.526 | 0.000 | 0.024 |
| CECR7 | −0.932 | 0.001 | 0.049 |
| CENPF | 1.176 | 0.000 | 0.041 |
| CES4A | 1.919 | 0.000 | 0.041 |
| CFD | −2.226 | 0.000 | 0.024 |
| CHODL | −4.067 | 0.000 | 0.020 |
| CHRDL1 | 3.451 | 0.000 | 0.014 |
| CHRFAM7A | 2.553 | 0.000 | 0.041 |
| CLDN1 | −2.065 | 0.001 | 0.049 |
| CLSTN2 | 2.887 | 0.000 | 0.006 |
| CNTN4 | −5.823 | 0.000 | 0.010 |
| COL22A1 | −5.561 | 0.000 | 0.019 |

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|---|---|---|---|
| COL8A1 | 1.850 | 0.000 | 0.040 |
| CPED1 | −1.193 | 0.000 | 0.019 |
| CSPG4P13 | −0.995 | 0.000 | 0.040 |
| CTSW | 3.543 | 0.000 | 0.040 |
| DIO2 | 1.512 | 0.000 | 0.027 |
| EDA2R | −0.967 | 0.000 | 0.040 |
| EEF1A2 | −3.087 | 0.000 | 0.018 |
| EFEMP1 | 1.972 | 0.000 | 0.014 |
| EGLN3 | 2.434 | 0.000 | 0.031 |
| EHBP1L1 | −0.830 | 0.001 | 0.047 |
| EPHA3 | −6.092 | 0.000 | 0.007 |
| EPHB6 | 5.366 | 0.000 | 0.016 |
| EPHX1 | −0.928 | 0.000 | 0.033 |
| EREG | −1.663 | 0.000 | 0.027 |
| EYA1 | −2.306 | 0.000 | 0.034 |
| FAM167A | 1.166 | 0.000 | 0.031 |
| FAM171A1 | 2.078 | 0.000 | 0.013 |
| FAM180A | 7.677 | 0.000 | 0.014 |
| FAM198B | 1.690 | 0.000 | 0.022 |
| FAM198B-AS1 | 2.419 | 0.000 | 0.040 |
| FAM43A | −1.285 | 0.000 | 0.042 |
| FBXO32 | 0.937 | 0.000 | 0.040 |
| FILIP1L | −1.272 | 0.000 | 0.023 |
| FLNC | −2.706 | 0.000 | 0.006 |
| FMNL1 | −1.727 | 0.000 | 0.023 |
| FMO6P | 2.394 | 0.000 | 0.031 |
| FRG1BP | −1.537 | 0.000 | 0.041 |
| FRG1CP | −0.831 | 0.001 | 0.049 |
| FRMD3 | 2.286 | 0.000 | 0.021 |
| FRZB | −2.818 | 0.000 | 0.008 |
| GALNT16 | −1.693 | 0.000 | 0.031 |
| GHR | −2.038 | 0.000 | 0.025 |
| GLB1L | −1.573 | 0.000 | 0.014 |
| GLP2R | 5.737 | 0.000 | 0.041 |
| GPR143 | −5.630 | 0.000 | 0.014 |
| GPRC5A | −0.951 | 0.001 | 0.049 |
| GREB1L | 1.464 | 0.000 | 0.038 |
| GRIA3 | 3.504 | 0.000 | 0.006 |
| GRID1 | −7.459 | 0.000 | 0.014 |
| H19 | 3.804 | 0.000 | 0.023 |
| HAGLR | −3.058 | 0.000 | 0.028 |
| HCAR1 | 3.204 | 0.000 | 0.019 |
| HDAC9 | −1.629 | 0.000 | 0.032 |
| HOXA9 | 1.258 | 0.000 | 0.040 |
| HOXB13 | −9.156 | 0.000 | 0.007 |
| HOXD9 | −4.882 | 0.000 | 0.038 |
| HS3ST3A1 | 2.829 | 0.000 | 0.020 |
| HS3ST3B1 | 2.865 | 0.000 | 0.006 |
| HSPB6 | −3.068 | 0.000 | 0.041 |
| HSPB7 | −4.167 | 0.000 | 0.018 |
| ID2 | 1.884 | 0.000 | 0.023 |
| IGDCC4 | −1.672 | 0.000 | 0.041 |
| IGF2 | 3.920 | 0.000 | 0.016 |
| IGFN1 | 6.423 | 0.000 | 0.014 |
| IL17RE | 2.597 | 0.000 | 0.036 |
| IRF4 | −4.794 | 0.000 | 0.023 |

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|---|---|---|---|
| KCNA3 | −4.644 | 0.000 | 0.032 |
| KCNK2 | 3.263 | 0.001 | 0.049 |
| KIAA1217 | −7.795 | 0.000 | 0.006 |
| KIAA1324L | 3.482 | 0.000 | 0.013 |
| KIAA1549 | 1.842 | 0.000 | 0.034 |
| KIAA1755 | −1.303 | 0.000 | 0.041 |
| KIF20A | 1.127 | 0.000 | 0.040 |
| KIT | 1.170 | 0.000 | 0.024 |
| KLF4 | −1.204 | 0.000 | 0.028 |
| L3MBTL4 | −2.143 | 0.000 | 0.028 |
| LANCL3 | 3.901 | 0.000 | 0.023 |
| LINC00987 | 2.001 | 0.000 | 0.042 |
| LINC01597 | −6.389 | 0.000 | 0.035 |
| LINGO1 | −1.950 | 0.000 | 0.028 |
| LRP5 | −1.804 | 0.000 | 0.032 |
| LRRC32 | 2.404 | 0.000 | 0.014 |
| LRRN3 | −1.662 | 0.000 | 0.022 |
| LYPD6B | 1.944 | 0.000 | 0.038 |
| LZTS1 | 0.911 | 0.001 | 0.049 |
| MAF | 2.860 | 0.000 | 0.013 |
| MAL | −4.804 | 0.000 | 0.023 |
| MCHR1 | 2.283 | 0.000 | 0.024 |
| MCOLN3 | −3.064 | 0.000 | 0.014 |
| MCTP2 | −6.413 | 0.000 | 0.035 |
| MEG3 | 3.478 | 0.000 | 0.014 |
| MEG9 | 3.475 | 0.000 | 0.018 |
| MFAP4 | 2.901 | 0.000 | 0.014 |
| MGP | 2.503 | 0.000 | 0.038 |
| MID2 | −1.467 | 0.000 | 0.044 |
| MKI67 | 0.842 | 0.000 | 0.041 |
| MLANA | −4.031 | 0.000 | 0.023 |
| MME | 0.926 | 0.000 | 0.032 |
| MOK | 1.034 | 0.000 | 0.045 |
| MS4A6E | −2.580 | 0.000 | 0.007 |
| MTSS1 | −3.194 | 0.000 | 0.040 |
| MT-TS1 | 0.892 | 0.000 | 0.042 |
| MYCL | 2.101 | 0.001 | 0.048 |
| NAP1L3 | −3.186 | 0.000 | 0.032 |
| NAV3 | −1.016 | 0.000 | 0.046 |
| NBPF22P | −2.582 | 0.000 | 0.042 |
| NBPF4 | −2.891 | 0.000 | 0.033 |
| NCEH1 | −0.994 | 0.000 | 0.038 |
| NDRG4 | −1.637 | 0.000 | 0.041 |
| NGFR | −4.556 | 0.000 | 0.038 |
| NOSIP | 1.342 | 0.000 | 0.022 |
| NPTX2 | −7.594 | 0.000 | 0.006 |
| NTN1 | −3.269 | 0.000 | 0.023 |
| NTRK2 | 1.311 | 0.000 | 0.038 |
| NUPR1 | 2.203 | 0.000 | 0.014 |
| NXPH4 | 2.261 | 0.000 | 0.027 |
| OLFM1 | 3.534 | 0.000 | 0.018 |
| OLFML2B | 1.869 | 0.000 | 0.014 |
| OLFML3 | −1.520 | 0.000 | 0.040 |
| OR1E1 | −8.410 | 0.001 | 0.048 |
| PAX9 | −6.157 | 0.000 | 0.032 |
| PAXIP1-AS2 | −1.964 | 0.000 | 0.022 |

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|---|---|---|---|
| PCBP3 | 1.488 | 0.000 | 0.024 |
| PCDH17 | −5.334 | 0.000 | 0.006 |
| PDE1C | 1.617 | 0.000 | 0.014 |
| PEAR1 | −4.338 | 0.000 | 0.006 |
| PID1 | −2.732 | 0.000 | 0.025 |
| PIM1 | 1.074 | 0.001 | 0.049 |
| PIP | 8.716 | 0.000 | 0.040 |
| PMEL | −0.962 | 0.000 | 0.040 |
| PODNL1 | 2.274 | 0.000 | 0.023 |
| PPP1R1C | −4.739 | 0.000 | 0.038 |
| PRELP | 1.823 | 0.000 | 0.033 |
| PROS1 | −0.843 | 0.000 | 0.045 |
| PTGDS | −4.541 | 0.000 | 0.012 |
| PTGFRN | 2.563 | 0.000 | 0.018 |
| PTGS1 | 5.011 | 0.000 | 0.006 |
| PTP4A3 | 2.422 | 0.000 | 0.016 |
| PTPRD | −4.112 | 0.000 | 0.034 |
| RAP2A | 0.884 | 0.000 | 0.039 |
| RARB | −2.438 | 0.000 | 0.019 |
| RARRES2 | 1.863 | 0.000 | 0.029 |
| RCAN2 | −1.365 | 0.000 | 0.034 |
| S100B | −3.243 | 0.000 | 0.027 |
| SEMA3F | 1.252 | 0.000 | 0.034 |
| SERPINB2 | −2.816 | 0.000 | 0.034 |
| SHANK2 | 1.726 | 0.000 | 0.038 |
| SHISAL1 | 2.629 | 0.000 | 0.024 |
| SIX2 | 1.927 | 0.000 | 0.032 |
| SLC15A3 | −6.289 | 0.000 | 0.012 |
| SLC1A3 | 1.194 | 0.000 | 0.034 |
| SLC38A5 | 3.235 | 0.000 | 0.016 |
| SLCO4A1 | 1.574 | 0.000 | 0.018 |
| SLFN11 | −1.501 | 0.000 | 0.018 |
| SNTB1 | −0.834 | 0.000 | 0.042 |
| SOBP | 1.792 | 0.000 | 0.037 |
| SOD3 | −1.719 | 0.000 | 0.040 |
| SORCS1 | −2.492 | 0.000 | 0.040 |
| SOX11 | 4.833 | 0.000 | 0.028 |
| ST8SIA2 | −0.834 | 0.000 | 0.045 |
| STAMBPL1 | 0.946 | 0.000 | 0.041 |
| STEAP4 | 2.175 | 0.000 | 0.006 |
| SYNE2 | 1.476 | 0.000 | 0.028 |
| TAC1 | 4.640 | 0.000 | 0.013 |
| TDRD9 | −3.793 | 0.000 | 0.012 |
| TEX11 | −2.812 | 0.000 | 0.023 |
| THBS2 | 1.280 | 0.001 | 0.049 |
| THY1 | 4.169 | 0.000 | 0.006 |
| TLE2 | 1.298 | 0.000 | 0.042 |
| TM4SF18 | −5.520 | 0.000 | 0.034 |
| TMEM132D | 5.580 | 0.000 | 0.014 |
| TMEM200C | −2.842 | 0.000 | 0.038 |
| TMEM204 | 1.071 | 0.000 | 0.034 |
| TNFSF15 | −1.394 | 0.000 | 0.022 |
| TP53I11 | 1.271 | 0.000 | 0.037 |
| TYRP1 | −2.472 | 0.000 | 0.008 |
| UNC5B | 3.350 | 0.000 | 0.006 |
| VSTM4 | 1.824 | 0.000 | 0.027 |

| | | | |
|---|---|---|---|
| ZBED6CL | 2.645 | 0.000 | 0.040 |
| ZEB1 | 1.143 | 0.001 | 0.049 |
| ZNF558 | −4.988 | 0.000 | 0.006 |
| ZNF560 | 3.943 | 0.000 | 0.032 |

**Table S2.** Enriched processes after RKIP silencing, specifying the False Discovery Rate for assignment and the list of genes for each one.

| TERM DESCRIPTION | FDR | MATCHING PROTEINS IN YOUR NETWORK (LABELS) |
|---|---|---|
| REGULATION OF BIOLOGICAL PROCESS | 0.0479 | ACE,ADAMTS12,ADAP1,ANLN,ARHGAP26,ARHGEF28,ARHGEF6,ATP10A,AURKC,BCL3,BST2,CAPG,CCDC3,CCL13,CD302,CD4,CDC25B,CDON,CENPF,CFD,CHODL,CHRDL1,CHRFAM7A,CLDN1,CLSTN2,CNTN4,COL8A1,CTCFL,DIO2,EDA2R,EEF1A2,EFEMP1,EGLN3,EPHA3,EPHB6,EREG,EYA1,FBXO32,FMNL1,FRZB,GHR,GLP2R,GPR143,GPRC5A,GRIA3,GRID1,HCAR1,HDAC9,HOXA9,HOXB13,HOXD9,HSPB6,HSPB7,ID2,IGF2,IL17RE,IRF4,KCNA3,KCNK2,KIAA1549,KIF20A,KIT,KLF4,L3MBTL4,LANCL3,LINGO1,LRP5,LRRC32,LRRN3,LYPD6B,LZTS1,MAF,MAL,MCHR1,MCTP2,MFAP4,MGP,MID2,MKI67,MOK,MTSS1,MYCL,NAV3,NCEH1,NDRG4,NGFR,NOSIP,NTN1,NTRK2,NUPR1,NXPH4,OLFM1,OR1E1,PAX9,PCBP3,PCDH17,PDE1C,PEAR1,PID1,PIM1,PIP,PODNL1,PPP1R1C,PROS1,PTGDS,PTP4A3,PTPRD,RAP2A,RARB,RARRES2,RCAN2,S100B,SEMA3F,SERPINB2,SHANK2,SIX2,SLC1A3,SLFN11,SORCS1,SOX11,SYNE2,TAC1,TDRD9,TEX11,THBS2,THY1,TLE2,TMEM132D,TMEM204,TNFSF15,TP53I11,TYRP1,UNC5B,ZEB1,ZNF558,ZNF560 |
| DEVELOPMENTAL AND DIFFERENTIATION PROCES | **0.0045** | ACE,ALPL,ANLN,ARHGAP26,ARHGEF28,AURKC,BCL3,BST2,CD4,CDC25B,CDO1,CDON,CENPF,CHODL,CHRDL1,CLDN1,CNTN4,COL8A1,EDA2R,EFEMP1,EPHA3,EREG,EYA1,FLNC,FRZB,GREB1L,HDAC9,HOXA9,HOXB13,HOXD9,HSPB7,ID2,IGF2,IRF4,KCNK2,KIAA1217,KIT,KLF4,LINGO1,LRP5,MAF,MAL,MCOLN3,MCTP2,MGP,MME,MTSS1,MYCL,NDRG4,NGFR,NOSIP,NTN1,NTRK2,NUPR1,OLFM1,OLFML3,PAX9,PCDH17,PID1,PIM1,PRELP,PTPRD,RAP2A,RARB,RARRES2,S100B,SEMA3F,SHANK2,SIX2,SLC1A3,SOBP,SOX11,ST8SIA2,STEAP4,SYNE2,TDRD9,TEX11,THY1,TLE2,TMEM204,TYRP1,UNC5B,ZEB1 |
| CELL SURFACE RECEPTOR SIGNALING PATHWAY | 0.0451 | ADAP1,ARHGEF28,BST2,CCL13,CD4,CDON,CHRDL1,EDA2R,EFEMP1,EPHA3,EPHB6,EREG,FRZB,GHR,GLP2R,GRIA3,GRID1,IGF2,IL17RE,IRF4,KIT,KLF4,LRP5,MCHR1,MTSS1,NGFR,NTRK2,PIM1,PODNL1,PTP4A3,PTPRD,SEMA3F,SERPINB2,THY1,TLE2,TNFSF15,UNC5B,ZEB1 |
| REGULATION OF CELL POPULATION PROLIFERATION | 0.0295 | ACE,CD4,CDC25B,CDON,EGLN3,EREG,EYA1,FRZB,GLP2R,ID2,IGF2,KCNK2,KIT,KLF4,LRP5,LRRC32,MTSS1,NDRG4,NGFR,NTN1,NTRK2,NUPR1,PID1,PIM1,RARB,S100B,SIX2,SOX11,TAC1,TP53I11,ZEB1 |
| CELLULAR RESPONSE TO CYTOKINE STIMULUS | 0.0443 | ADAMTS12,BST2,CCL13,CD4,CLDN1,EDA2R,EREG,GHR,IL17RE,IRF4,KIT,KLF4,MME,NGFR,PID1,PIM1,PODNL1,PTP4A3,SERPINB2,TNFSF15,ZEB1 |
| BEHAVIOR | 0.0183 | GRID1,HOXD9,ID2,KCNK2,KIT,MCHR1,MCOLN3,NDRG4,NPTX2,NTRK2,PCDH17,S100B,SHANK2,SLC1A3,SOBP,TAC1 |
| REGULATION OF PEPTIDYL-TYROSINE PHOSPHORYLATION | 0.0443 | ACE,CD4,EREG,GHR,GPRC5A,IGF2,KIT,NTRK2,THY1 |
| DEVELOPMENTAL PIGMENTATION | 0.0401 | GPR143,KIT,PMEL,TYRP1, MLANA |
| POSITIVE REGULATION OF INTERLEUKIN-10 BIOSYNTHETIC PROCESS | 0.0331 | BCL3,IRF4 |

**Table S3.** Genes related with development process, which are potentially targets of NANOG transcription factor.

| TERM DESCRIPTION | FDR | MATCHING PROTEINS IN YOUR NETWORK (LABELS) |
|---|---|---|
| Genes targeted by NANOG | 4. 21 × $10^{-9}$ | ALPL,ANLN,ARHGAP26,AURKC,BCL3,BST2,CD4,CENPF,CLDN1,CNTN4,COL8A1,EDA2R,EPHA3,EREG,EYA1,FRZB,GREB1L,HOXA9,HOXB13,HSPB7,ID2,IGF2,UNC5B,KCNK2,KIAA1217,KIT,KLF4,MAL,MCOLN3,MME,MTSS1,NDRG4,NGFR,NOSIP,NTN1,NTRK2,NUPR1,OLFM1,OLFML3,TLE2,THY1,TEX11,PAX9,PCDH17,PID1,PIM1,PRELP,PTPRD,RAP2A,RARB,SEMA3F,SHANK2,SLC1A3,SOBP,SOX11,ST8SIA2,STEAP4,SYNE2,TDRD9 |