

Supplemental Figure 1. miRs that are not downregulated by ZEB1 have metastasis suppressor activity. (A) Kaplan Meier plots showing the miR levels that are correlated positively with longer survival durations. (B) qPCR analysis of miR expression levels in KP cell lines classified as epithelial or mesenchymal 1. P values are indicated for those miRs that reach statistical significance. A ZEB1 target, miR-200b, was included as a positive control. (C) qPCR analysis of epithelial (CDH1) and mesenchymal (ZEB1, TWIST1, SNAI1, SNAI2, CDH2 and VIM) markers in 393P cells transfected with the indicated antagomirs or negative control (anti-NC). (D) qPCR assays to quantify ectopic miR expression in H 1299 cells stably transfected with the corresponding miRs or empty vector. Results expressed relative to empty vector (Vec). (E) Boyden chamber assays of H1299 cells that express ectopic miRs or empty vector. Migratory cells were photographed (images) and counted (bar graphs). Results are expressed relative to empty vector transfectants. Scale bar: $200 \mu \mathrm{~m}$. Values are Mean $\pm$ SD. $\mathrm{n}=3$. P values, 2 -tailed Student's t-test and Dunnett's test for 2 -group and $>2$-group comparisons. Results were replicated ( $\mathrm{n} \geq 2$ experiments).


Supplemental Figure 2. Characterization of miR-181b transfectants. (A) Quantitative RT-PCR (qPCR) analysis of miR-181b levels in 344SQ and H1299 cells stably transfected with miR-181b or empty vector (Vec). (B) qPCR analysis of miR-181b levels in 344SQ_RFP cells transfected with miR-181b or empty vector (Vec). (C) Relative densities of 344SQ and H1299 transfectants in monolayer culture as assessed by the WST-1 method. n=4. (D) qPCR analysis of miR-181b levels in 393P_EGFP cells treated with antagomir-181b or negative control oligomers (anti-NC). Values are Mean $\pm$ SD. $n=3$, unless otherwise indicated. $P$ values, 2 -tailed Student's $t$-test. Results were replicated ( $\mathrm{n} \geq 2$ experiments).


Supplemental Figure 3. AntagomiR-181b promotes the migration of lung cancer cells with low but not high endogenous ZEB1 levels. (A) Quantitative RT-PCR (qPCR) analysis of miR-181b levels in KP cells treated with antagomir-181b or negative control oligomers (anti-NC). (B) qPCR analysis of miR-181b levels in lung cancer cells stably transfected with ZEB1 or empty (Vec) expression vectors after treatment with antagomir-181b or antiNC. (C) Boyden chamber assays of cells in (B). Migratory cells were photographed (images) and counted (bar graphs). Results are expressed relative to negative controls (anti-NC). Scale bar: $200 \mu \mathrm{~m}$. Values are Mean $\pm$ SD. $n=3$. P values, 2 -tailed Student's $t$-test. Results were replicated ( $\mathrm{n} \geq 2$ experiments).


Supplemental Figure 4. ITGA1 promotes metastasis. (A) Quantitative RT-PCR (qPCR) analysis of predicted miR-181b targets that were the most highly upregulated by ectopic ZEB1 expression in 393P cells. P values are indicated for those miRs that are significantly different between epithelial and mesenchymal KP cells. (B) Scatter plot of normalized gene expression levels (ITGA1 versus ZEB1) in a compendium of 1,016 human lung adenocarcinomas in The Cancer Genome Atlas (dots). Correlation r-value by Pearson's. (C) qPCR analysis of ITGA1 mRNA in 344SQ cells stably transfected with scrambled control shRNA (shCTL) or 1 of 2 distinct ITGA1 shRNAs (shITGA1). Results expressed relative to shCTL. (D) Primary tumor weights and numbers of lung metastases in syngeneic mice injected subcutaneously with 344SQ cells stably transfected with 1 of 2 distinct ITGA1 shRNAs (shITGA1) or control shRNA (shCTL). (E) qPCR analysis of ITGA1 levels in 344SQ_RFP cells stably transfected with shITGA1 or shCTL. Results expressed relative to shCTL transfectants. (F) Fluorescence microscopic image of RFP-positive tumors on the lung surface. Scatter plot of lung metastasis numbers per mouse (dots) following tail vein injection. Values are Mean $\pm$ SD. $n=3$, unless otherwise indicated. $P$ values, 2 -tailed Student's $t$-test and Dunnett's test for 2 -group and $>2$ group comparisons. Results were replicated ( $\mathrm{n} \geq 2$ experiments).


Supplemental Figure 5. Ectopic expression of ITGA1 3'UTR constructs. (A) Schematic illustration of constructs used in Figure 3E that express wild-type ITGA1 coding sequences with the 3'UTR (CDS_UTR) or without the 3'UTR (CDS) or that has a mutation (ATG to TAA) in the translation start codon (CDSMT_UTR). (B) Western blot analysis (WB) to detect ectopic ITGA1 protein (top) and RT-PCR analysis (RT-PCR) to detect the ectopic CDS or 3'UTR RNAs. 344SQ_RFP cells were stably transfected with constructs in (A) and transiently transfected with scrambled control siRNA (siCTL) or an ITGA1 siRNA (silTGA1) that targets 3'UTR sequences to deplete endogenous ITGA1 mRNA but not the ectopic CDS or 3'UTR. $\alpha$-tubulin and $\beta$-actin included as loading controls. (C) qPCR analysis of ectopic ITGA1 3'UTR expression in 393P cells stably transfected with vectors that express wild-type (UTR-WT) or miR-181b binding sitemutated 3'UTR (UTR-MT). Values are Mean $\pm$ SD. $n=3$. P values, Dunnett's test. Results were replicated ( $n \geq 2$ experiments).


Supplemental Figure 6. Zeb1 upregulates ITGA1 expression through multiple intermediates. (A) RNA Pol II chromatin immunoprecipitation assays of the ITGA1 gene promoter in 393P_ZEB1 cells (ZEB1) and 393P_vector cells (Vec). Values are expressed relative to the IgG control. (B) Quantitative RT-PCR (qPCR) analysis of ITGA1 and ZEB1 levels before ( $\mathrm{t}=0$ ) and each day after the start of doxycycline treatment in 393P cells that express doxycycline-inducible ZEB1. A ZEB1 target, miR-200b, was included as a positive control. (C) Quantitative RT-PCR (qPCR) analysis of mRNA levels after treatment with vehicle (CTL) or 5-azacytidine (5-Aza). (D-F) qPCR analysis of mRNAs in KP cells classified as epithelial or mesenchymal. (G) qPCR analysis of mRNAs in 393P cells transiently transfected with siRNAs against DNMT1 (siDNMT1), DNMT3B (siDNMT3B), or scrambled control (siCTL). (H and I) Western blot analysis (E) and qPCR analysis of ITGA1 mRNA (F) in 344SQ cells transiently transfected with Myc-tagged DNMT1 or DNMT3B. Ectopic DNMT protein detected using an anti-Myc antibody. Anti-a-tubulin antibody included as a loading control. (J) Schema, luciferase reporters driven by ITGA1 promoter fragments. Bar graph, luciferase activities in 393P cells co-transfected with reporters and ZEB1 or empty (Vec) expression vector. (K) qPCR analysis of ARNT mRNA levels in KP cells classified as epithelial or mesenchymal. (L) Western blot analysis of ARNT protein levels in KP cells classified as epithelial (E) or mesenchymal (M). $\beta$ actin was used as a loading control. (M) qPCR analysis of ARNT mRNA levels in 393P ZEB1 cells (ZEB1) and 393P Vec cells (Vec). (N) qPCR analysis of ITGA1 mRNA levels in 393P_ZEB1 cells transiently transfected with miR-148a or non-coding control (miR-NC). (O) qPCR analysis of miRs in 393P_ZEB1 cells (ZEB1) and 393P vector cells (Vec). Values are Mean $\pm$ SD. $n=3$, unless otherwise indicated. $P$ values, 2-tailed Student's $t$-test and Dunnett's test for 2-group and > 2-group comparisons. Results were replicated ( $n \geq 2$ experiments).

A


ONECUT2


TGFBR3


BHLHE41


B


E


C

$D$


F





Correlation
(vs. ITGA1)
$\mathrm{R}=0.860, P=0.0003$
R=1.000, $P=0.0000$
$\mathrm{R}=0.902, P<0.0001$

Supplemental Figure 7. ITGA1 and ADCY9 compete for binding to miR-181b. (A) Quantitative RT-PCR (qPCR) analysis of mRNAs. P values are indicated for those mRNAs that are significantly different between KP cell lines classified as epithelial or mesenchymal. (B and C) qPCR analysis of ITGA1 (B) and ADCY9 (C) mRNA levels in 344SQ cells co-transfected with siRNA against the 3'UTR of ITGA1 (siUTR) or control siRNA (siCTL) and a vector that expresses ITGA1 coding sequence (CDS) or nothing (Vec). (D) ITGA1 3'UTR reporter activities in 344SQ cells transiently co-transfected with ITGA1 siRNA (silTGA1) or control siRNA (siCTL) and the indicated 3'UTR reporter constructs. (E and F) ADCY9 mRNA (E) and AC9 protein (F) levels in 393P cell transfectants by qPCR and WB, respectively. (G) qPCR analysis of ADCY9 and ITGA1 mRNA levels in 344SQ cells co-transfected with scrambled siRNAs (siCTL) or ADCY9 siRNAs (siADCY9) and ADCY9 3'UTR (ADCY9UTR) or EGFP control expression vectors. (H) qPCR analysis of ITGA1 mRNA levels in 393P cells transfected with wild-type ADCY9 3'UTR (WT) or mutant ADCY9 3'UTR lacking miR-181b binding sites (MT) or EGFP expression vectors. (I) A heat map showing the expression pattern of ZEB1, ITGA1, and ADCY9 in KP cell lines classified as epithelial ( E ) or mesenchymal ( M ). Pearson correlation analysis was performed. Values are Mean $\pm$ SD. $n=3$. P values, 2-tailed Student's $t$-test and Dunnett's test for 2 -group and > 2-group comparisons. Results were replicated ( $\mathrm{n} \geq 2$ experiments).


Supplemental Figure 8. ADCY9 increases cyclic AMP production and promotes tumor cell migration and invasion. (A-C) Cyclic AMP levels in: (A) KP cell lines classified as mesenchymal or epithelial; (B) 393P_ZEB1 cells (ZEB1) and 393P_vector cells (Vec); (C) 393P cells treated with forskolin (FSK) or the vehicle dimethylsulfoxide (DMSO). (D) Boyden chamber assays of 393P cells treated with FSK or DMSO. Migratory cells were photographed (images) and counted (bar graphs). Results are expressed relative to controls. Scale bar: $200 \mu \mathrm{~m}$. (E) qPCR analysis of ADCY9 mRNA levels in 344SQ_RFP cells transfected with ADCY9 siRNA (siAC9) or scrambled siRNAs (siCTL). Results are expressed relative to siCTL transfectants. (F) Boyden chamber migration assays of 344SQ and H1299 cells co-transfected with miR-181b or control miR mimic and ADCY9 or empty (Vec) expression vector. Migratory cells were photographed (images) and counted (bar graphs). Results are expressed relative to controls. Scale bar: $200 \mu \mathrm{~m}$. (G) Western blot (WB) and RT-PCR analysis of 344SQ cells transfected with (+) or without (-) ADCY9 siRNA (siADCY9), scrambled siRNA (siCTL), ADCY9 coding sequence (CDS), ADCY9 3'UTR (UTR), or empty vector (Vec). (H) Boyden chamber assays of 344SQ cell transfectants from (G). Migratory cells were photographed (images) and counted (bar graphs). Results are expressed relative to controls. Scale bar: $200 \mu \mathrm{~m}$. Values are Mean $\pm$ SD. $\mathrm{n}=3$, unless otherwise indicated. P values, 2-tailed Student's t-test and Dunnett's test for 2-group and > 2-group comparisons. Results were replicated ( $\mathrm{n} \geq 2$ experiments).


Supplemental Figure 9. Expression and biological roles of ADCY isoforms in KP cells. (A) Expression levels of ADCY (AC) mRNAs in 393P_Vector cells and 393P_ZEB1 cells determined by RNA-seq. Results expressed as reads per kilobase of transcript per million mapped reads (RPKM). (B) qPCR analysis of AD $\bar{C} Y 3$ (left) and ADCY7 (right) mRNA levels in 344SQ cells transfected with ADCY3 siRNA (siAC3) or ADCY7 siRNA (siAC7) or siCTL
Results are expressed relative to siCTL transfectants. (C) Cyclic AMP levels in 344SQ cells transfected with siAC3, siAC7, or siCTL. (D) Boyden chamber assays of 344SQ cells transfected with siCTL or siAC7. Migratory cells were photographed (images) and counted (bar graphs). Results are expressed relative to siCTL transfectants. Scale bar: $200 \mu \mathrm{~m}$. (E) Relative densities of 344SQ cells transfected with siAC7 or siCTL in monolayer culture as assessed by the WST-1 method. $n=4$. (F) Boyden chamber assays of 344SQ cells transfected with siCTL or siAC3. Migratory cells were photographed (images) and counted (bar graphs). Results are expressed relative to siCTL transfectants. Scale bar: $200 \mu \mathrm{~m}$. (G) Relative densities of 344SQ cells transfected with siAC3 or siCTL in monolayer culture as assessed by the WST-1 method. $n=4$. Values are Mean $\pm$ SD. $n=3$, unless otherwise indicated. $P$ values, 2 -tailed Student's t-test and Dunnett's test for 2-group and > 2-group comparisons. Results were replicated ( $\mathrm{n} \geq 2$ experiments).


Supplemental Figure 10. ADCY9 does not induce EMT but activates a poor-prognosis expression signature in lung cancer. (A) qPCR validation of genes found by Affymetrix profiling to be upregulated (left bar graph) or downregulated (right bar graph) by ectopic ADCY9 expression in 393P cells. (B and C) qPCR analysis of mRNA levels of markers of epithelial (CDH1) and mesenchymal (ZEB1, SNAI1, SNAI2, TWIST1, CDH2, VIM) differentiation in 393P_ADCY9 cells (AC9) and 393P_vector cells (Vec) (B) or 344SQ cells transfected with siCTL or 1 of 2 ADCY9 siRNAs (C). Results are expressed relative to $\mathrm{Vec}(\mathbf{B})$ and siCTL (C) transfectants. (D) Kaplan-Meier analysis of lung cancer patients, comparing the differences in risk between tumors with high ("top third"), intermediate, or low ("bottom third") t-scores that reflect the degree of overlap with the 1,421-gene expression signature. Log rank test (Log rank p) evaluates differences between two arms. Values are Mean $\pm$ SD. $n=3$, unless otherwise indicated. P values, 2-tailed Student's $t$-test and Dunnett's test for 2group and $>2$-group comparisons. Results were replicated ( $\mathrm{n} \geq 2$ experiments).

Supplementary Table 1

|  | Correlation coefficient |  |  | $P$ value |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Cancer | $\begin{gathered} \text { ADCY9 } \\ \text { vs. } \\ \text { ITGA1 } \end{gathered}$ | $\begin{gathered} \hline \text { ADCY9 } \\ \text { vs. } \\ \text { ZEB1 } \end{gathered}$ | $\begin{aligned} & \text { ITGA1 } \\ & \text { vs. } \\ & \text { ZEB1 } \end{aligned}$ | $\begin{gathered} \text { ADCY9 } \\ \text { vs. } \\ \text { ITGA1 } \\ \hline \end{gathered}$ | $\begin{gathered} \hline \text { ADCY9 } \\ \text { vs. } \\ \text { ZEB1 } \end{gathered}$ | $\begin{gathered} \text { ITGA1 } \\ \text { vs. } \\ \text { zEB1 } \end{gathered}$ |
| ACC | 0.371300768 | 0.393727558 | 0.120483507 | 0.000754738 | 0.000330798 | 0.290205695 |
| BLCA | 0.453964941 | 0.485035176 | 0.754298922 | 3.90E-22 | $1.83 \mathrm{E}-25$ | 3.35E-76 |
| BRCA | 0.163876597 | 0.299120903 | 0.768174823 | 4.93825E-08 | $4.53 \mathrm{E}-24$ | 6.75E-214 |
| CESC | 0.018469113 | 0.042712944 | 0.582454101 | 0.748422031 | 0.458089572 | 5.23E-29 |
| CHOL | 0.124297352 | -0.055910382 | 0.623011932 | 0.470127038 | 0.746031373 | $4.9452 \mathrm{E}-05$ |
| CRC | 0.096102511 | 0.221989007 | 0.706858057 | 1.64E-02 | $2.15 \mathrm{E}-08$ | 1.91E-95 |
| DLBC | 0.39525568 | 0.532669137 | 0.563380419 | 0.005428558 | $9.73 \mathrm{E}-05$ | 3.06E-05 |
| ESCA | 0.207041952 | 0.264945076 | 0.734902611 | 0.004803331 | $2.78 \mathrm{E}-04$ | 1.61E-32 |
| GBM | 0.226577313 | 0.206631372 | 0.210841649 | 0.003849629 | 0.008541669 | 0.007259847 |
| HNSC | 0.258010356 | 0.314444946 | 0.789367133 | $2.3614 \mathrm{E}-09$ | $2.13 \mathrm{E}-13$ | 7.75E-112 |
| KICH | -0.079396631 | 0.040897766 | 0.33900585 | 0.526277488 | 0.744391673 | 0.005361976 |
| KIRC | 0.36086756 | 0.296517452 | 0.767771417 | $7.75 \mathrm{E}-18$ | $2.80205 \mathrm{E}-12$ | $9.90 \mathrm{E}-105$ |
| KIRP | 0.086527109 | -0.076459454 | 0.591369183 | 0.141589458 | 0.194172098 | $9.64 \mathrm{E}-29$ |
| LAML | 0.037756318 | -0.245705611 | -0.016426209 | 0.621883606 | 0.001120336 | 0.830156207 |
| LGG | 0.225548888 | 0.043999326 | 0.197481779 | $2.24362 \mathrm{E}-07$ | 0.318506449 | 6.19481E-06 |
| LIHC | 0.393447577 | 0.239384051 | 0.491857534 | $3.48 \mathrm{E}-15$ | $3.11213 \mathrm{E}-06$ | 5.37E-24 |
| LUAD | 0.107844485 | 0.280283311 | 0.557525511 | 0.0143421 | $9.45457 \mathrm{E}-11$ | 2.13E-43 |
| LUSC | 0.295068055 | 0.324961737 | 0.703961405 | $1.60 \mathrm{E}-11$ | $8.73 \mathrm{E}-14$ | 3.59E-76 |
| MESO | 0.08540522 | 0.080209663 | 0.483101988 | 0.431560847 | 0.460200918 | $2.14 \mathrm{E}-06$ |
| OV | 0.130306668 | 0.273563308 | 0.639833267 | 0.035021563 | $7.03 \mathrm{E}-06$ | $1.43 \mathrm{E}-31$ |
| PAAD | 0.323634817 | 0.335222617 | 0.814849085 | 1.05E-05 | $4.79 \mathrm{E}-06$ | $1.54 \mathrm{E}-43$ |
| PCPG | 0.091605695 | 0.296435866 | 0.155400442 | 0.222623977 | $5.60 \mathrm{E}-05$ | 0.037784356 |
| PRAD | 0.59579456 | 0.547776047 | 0.823481832 | 4.45E-49 | $2.93 \mathrm{E}-40$ | 6.19E-124 |
| SARC | 0.477786885 | 0.349290501 | 0.397418396 | 3.55E-16 | 7.60035E-09 | $3.12801 \mathrm{E}-11$ |
| SKCM | -0.21714274 | -0.318660976 | 0.658592344 | $2.06726 \mathrm{E}-06$ | $1.58 \mathrm{E}-12$ | 1.19E-59 |
| STAD | 0.49119428 | 0.562750918 | 0.761153463 | 1.37E-26 | $4.90 \mathrm{E}-36$ | 1.12E-79 |
| TGCT | 0.598214135 | 0.391715669 | 0.48182847 | $6.29 \mathrm{E}-16$ | 7.16E-07 | $4.31 \mathrm{E}-10$ |
| THCA | 0.43621786 | 0.305125625 | 0.797880951 | 8.82E-25 | $2.68 \mathrm{E}-12$ | $3.32 \mathrm{E}-112$ |
| THYM | 0.597308851 | -0.227587608 | -0.071254535 | 5.97E-13 | 0.012422848 | 0.439304599 |
| UCEC | 0.039590203 | 0.167767068 | 0.59395272 | 0.356277095 | $8.3025 \mathrm{E}-05$ | 2.88E-53 |
| UCS | 0.103090071 | 0.503261857 | 0.186944163 | 0.445400028 | 6.60E-05 | 0.163789592 |
| UVM | -0.149424309 | -0.149217401 | 0.794379398 | 0.185869348 | 0.186486286 | $1.46 \mathrm{E}-18$ |

## Supplementary table 3

| qPCR primers |  |  |
| :---: | :---: | :---: |
| Gene | Forward ( $5^{\prime}-3{ }^{\prime}$ ) | Reverse (5'-3') |
| Itga1 (mouse) | TGGCTTCTCACCGTTATCCTA | CACACAAGGCATTGATCTCTCT |
| ITGA1(human) | CCGAAGAGGTACTTGTTGCAGC | GGCTTCCGTGAATGCCTCCTTT |
| Rpl32(mouse) | GGAGAAGGTTCAAGGGCCAG | TGCTCCCATAACCGATGTTTG |
| RPL32 (human) | CCTTGTGAAGCCCAAGATCG | TGCCGGATGAACTTCTTGGT |
| Zeb1 (mouse) | GCTCAGCCAGGAACCCGCAG | TGGGCACCCTCTGCCACACA |
| Dnmt1 (mouse) | GGACAAGGAGAATGCCATGAAGC | TTACTCCGTCCAGTGCCACCAA |
| Dnmt3a (mouse) | CGCAAAGCCATCTACGAAGTCC | GCTTGTTCTGCACTTCCACAGC |
| Dnmt3b (mouse) | CGCACAACCAATGACTCTGCTG | GGTGACTTCAGAAGCCATCCGT |
| Tet1 (mouse) | TCACAACATGCACAACGGA | GGTTGGCCCATTGACTTG |
| Tet2 (mouse) | ACCTGGCTACTGTCATTGCTCC | TGCAGTGACTCCTGAGAATGGC |
| Tet3 (mouse) | GCAGAAGGAGAAACTGAGCAC | CTTAAAGGAGCTAAAGTGGTTCTGAG |
| Arnt (mouse) | CTCACGAAGGTCGTTCATCTGC | CCACAAAGTGAGGTTCTCCTTCC |
| Fgd4 (mouse) | CCTCAAACTAGCAGCTCGGAAC | GAGCCAACCAAGCTGAATCTGG |
| Sema4g (mouse) | TTCATGGAGCGTGAGGAAGGCT | TGGCAGATGAGACGAGCCTTCA |
| Pkdcc (mouse) | AGCTGTTGCAGACTTCCTGGGA | CCGTTCACTAGCACAAACTGCC |
| Thrb (mouse) | ACCACTATCGCTGCATCACCTG | ACTGGTTGCGGGTGACTTTGTC |
| Nmnat2 (mouse) | TGTCAAGTCGGCACCGTCTCAT | ATCAGGTCTCGATGGTGCTCCA |
| Evi2a(mouse) | CTTCTGGACAGCAAGCATCACC | TGAGGCAAGGAGTTGTTGACCG |
| Plcl2(mouse) | GGAACGGAAACTACAGAAGGCAG | GTGGATCTGCTTCAGGTTCTCC |
| Onecut2(mouse) | TTCCAGCGCATGTCTGCCTTAC | GAAGATGGCGAAGAGTGTTCGG |
| Trim2(mouse) | CACGAACCTCATGGATGTGCTG | GGTCTCACAGGACTGGCAGTAA |
| Vcan (mouse) | GGACCAAGTTCCACCCTGACAT | СTTCACTGCAAGGTTCCTCTTCT |
| Sipa112(mouse) | GACGTGATTGGCTGGACTTCAG | GTCATTTCCACAGTCTCGCAGC |
| Adcy9(mouse) | GCAAAATGGCTGTCAAGACGAGC | CTGGCTGTTAGTGAGCTTCTCC |
| Mfsd6(mouse) | TGAGCTGAGGACTTCTGCACAG | TGCCAATCCCTCGGAAAGTTGC |
| Megf9(mouse) | GGTGCGAGAAATGCCTAGAAGG | GCACTGATGTGGTCAAAGAGGC |
| Zfhx4(mouse) | AGCCTTGACAGCAGAGGGTTCT | GCTCCtTtGCTGGCTTCTGTTC |
| Hoxb4(mouse) | CTGGATGCGCAAAGTTCACGTG | GCGTCAGGTAGCGATTGTAGTG |
| Itsn1(mouse) | TGCTCCTTTGCCAGTGACCTCT | TCTGGCTTCTCGTTTGAGCTGC |
| Pax9(mouse) | ATCCGCTCCATCACCGACCAAG | ССтTСTССААТССАTTCACTGCG |
| Dock4(mouse) | GATAGGAGAGGTGGATGGCAAG | CGCCtTGAGATGCAGATCGTAG |
| Mb21d2(mouse) | GGAATACGACGACCAGAGAGCG | GAGAGCAACAGATACTCGTTGGC |
| Fos (mouse) | GGGAATGGTGAAGACCGTGTCA | GCAGCCATCTTATTCCGTTCCC |
| Asah2(mouse) | GTGACAACGACAAGAGCACCTG | GCCTTCTGATAGATGATCCGTCC |
| Nsun3(mouse) | CTGTTCTCGTCGGACTCTCAGA | TCAGCCTTGGAAAGCGTGCATG |
| G6pc3(mouse) | CCTTCATTGCTGAGTGGCTCAAC | CCTGGACCAGTCTCACAAGAAG |
| Dip2c(mouse) | CAGATAGAGGACAATGACCAGGC | CCGACAGTTGAGCAGAGTGTAC |
| Cnksr3(mouse) | ATGGATGCCTCCCTGAAGAAGG | GTGTCCTCTGTAGCCGAAACTC |
| Iqgap2(mouse) | CGCCAGGAATATCTGCACAGAC | CTTCCTTGCTGTCACCATTCGG |
| Tmed8(mouse) | ATAACCGTGCAGGTCAGTGACTC | AGAACTCCTGGAGCCTCTCTCT |
| Bhlhe41(mouse) | GGCATTTGGAGAAAGCAGTAGTC | AGTGGAACGCATCCAAGTCGGC |
| Adcy3 (mouse) | CCTCTGAGGATGAGCACGAACT | GAGTAGCGTGTTTCCATCTCTGG |
| Adcy7 (mouse) | GACGAGATGCTGTCAGCCATTG | CACGCTCAAAGCCCTTCTCCAA |
| Rnf150 (mouse) | GCTCCAACACAAACGAGACCATC | CCTTTCCAGCAGGCTCACTATC |
| Rnf125 (mouse) | TGTCAGCGGGAACTGGATGAAG | CAGGTCGTGAATGGCAAAGTGG |
| stc1 (mouse) | AGGAGGACTGCTACAGCAAGCT | TCCAGAAGGCTTCGGACAAGTC |
| Plcb1 (mouse) | CGCTGAGGAAGAGCCTGTCATT | GTCTTGAACGCACACTCTGCGA |
| Csn3 (mouse) | CTACTTCTGCTTAGGTCTCCAGC | GGTTGGAATGGCGGTGTTATCC |
| Aspm (mouse) | GCAAAGGAAGTTGCGGATGCTG | TAGTGCTTCAACCTCAGAAACCG |


| Bub1 (mouse) | TGCCACAGTGTGGACCAGAAAC | GACAGTTGGTGATGGCTGCACT |
| :---: | :---: | :---: |
| Prr11 (mouse) | ACCAGAGGAACGCACTCCACTA | CTACCTGGACTTTTTCTCAGCAGC |
| Mki67 (mouse) | GAGGAGAAACGCCAACCAAGAG | TTTGTCCTCGGTGGCGTTATCC |
| Cenpe (mouse) | AGGATCATGCCACCGAGAAGAC | GCTGTGTCTCTTGGAGTTTCTGG |
| Pbk (mouse) | CTCAGAGTTGCTTTGCACATGGC | CATCCAATGGCAGAGAGACTCC |
| Ccna2 (mouse) | TTGTAGGCACGGCTGCTATGCT | GGTGCTCCATTCTCAGAACCTG |
| Kif2c (mouse) | CTGTGCCTACAAACTCTCGCAAG | TGCTCTTCTGCCTCCTCACTGA |
| Depdc1a (mouse) | AGCTCGGAGAGTCTAGTACCAC | ССтСTСTAAGTGAGGTTGCAGC |
| Timp3 (mouse) | AGGATGCCTTCTGCAACTCCGA | GTGTAGACCAGAGTGCCAAAGG |
| Antxr1 (mouse) | CGGATTGCAGACAGTAAGGACC | GGATGGTTCAGCCGCCAGAATT |
| Sema3d (mouse) | TAGACACGCACAACCTGGAGTC | GCTGTTCCAGAGTAGAGGTGCT |
| Isir (mouse) | CCAATGTGACCACACTGAGCCT | AATAGCCACCGAGCGGATCTCA |
| Elfn1 (mouse) | ATCGTTCACCGTGTCCAAGCTG | GCTGGTAGAGACCACGCAGTAT |
| Atoh8 (mouse) | CAACGGAGATCAAAGCCCTGCA | CTTCTGCCCATAGGAGTAGCAC |
| Mgst1 (mouse) | TGCGACCGCATTCCAGAGGATA | TCCACCTTCTCGTCAGTGCGAA |
| Sptssb (mouse) | TGCTGTCATGGAGCCTTGGGAA | ATTCCCAAGCCAGGCGGATGTG |
| Grhl3 (mouse) | GTCCAGCACATTGAAGAGGTGG | TGCGAGGAGAAGTCTGTGCTCA |
| Rasl11a (mouse) | GATTCATCGGCGACTACGAACC | CGGAGTGTCCTGGATCTGTAGG |
| ChIP PCR primers |  |  |
| Pol II ChIP primers | AAGATCGCCCTCTCAGTGAA | CTGTCCGAGACATGGACAAA |
| ARNT ChIP primers $(+200)$ | CCATCTGGGATCTGAGAAGC | GACGCCTGGGGACCAT |
| ARNT ChIP primers $(+1 \mathrm{k})$ | GTGGCACCCTTCTCCTACTTT | CCTGGTCACTCATGATCCC |
| DNA methylation related primers |  |  |
| BSP primers | TTTAGTGAAAGGTAGATGTTTTTTTAAG | TACTAATTCRTAAACAAAAACTAACAAAA |
| miRNA qPCR RT primers |  |  |
| miR-148a-RT | GTCGTATCCAGTGCAGGGTCCGAGGTATTCGCACTGGATACGACACAAAG |  |
| U6-RT | GTCGTATCCAGTGCAGGGTCCGAGGTATTCGCACTGGATACGACAAAATATG |  |
| miR-181a-RT | GTCGTATCCAGTGCAGGGTCCGAGGTATTCGCACTGGATACGACACTCAC |  |
| miR-181b-RT | GTCGTATCCAGTGCAGGGTCCGAGGTATTCGCACTGGATACGACACCCAC |  |
| miR-218-5p-RT | GTCGTATCCAGTGCAGGGTCCGAGGTATTCGCACTGGATACGACACATGG |  |
| miR-342-3p-RT | GTCGTATCCAGTGCAGGGTCCGAGGTATTCGCACTGGATACGACACGGGT |  |
| let-7f-1-3p-RT | GTCGTATCCAGTGCAGGGTCCGAGGTATTCGCACTGGATACGACGGGAAG |  |
| miR-150-5p-RT | GTCGTATCCAGTGCAGGGTCCGAGGTATTCGCACTGGATACGACCACTGG |  |
| miR-425-3p-RT | GTCGTATCCAGTGCAGGGTCCGAGGTATTCGCACTGGATACGACGGCGGA |  |
| miR-26a-1-3p-RT | GTCGTATCCAGTGCAGGGTCCGAGGTATTCGCACTGGATACGACCGTGCA |  |
| mir-130a-3p-RT | GTCGTATCCAGTGCAGGGTCCGAGGTATTCGCACTGGATACGACATGCCC |  |
| miRNA qPCR primers | Forward ( $5^{\prime}-3^{\prime}$ ) | Reverse ( $5^{\prime}$ '3') |
| U6 | GCGCGTCGTGAAGCGTTC | GTGCAGGGTCCGAGGT |
| miR-148a | CGCGTCAGTGCACTACAGAAC | GTGCAGGGTCCGAGGT |
| miR-181a | CATTCAACGCTGTCGGTG | GTGCAGGGTCCGAGGT |
| miR-181b | AACATTCATTGCTGTCGGTGG | GTGCAGGGTCCGAGGT |
| miR-218-5p-rltm | CGCGTTGTGCTTGATCTAAC | GTGCAGGGTCCGAGGT |
| miR-342-3p-rltm | CGTCTCACACAGAAATCGCA | GTGCAGGGTCCGAGGT |
| let-7f-1-3p-rltm | GCGCGCTATACAATCTATTGC | GTGCAGGGTCCGAGGT |
| miR-150-5p-rltm | CGTCTCCCAACCCTTGTAC | GTGCAGGGTCCGAGGT |
| miR-425-3p-rltm | CGATCGGGAATGTCGTG | GTGCAGGGTCCGAGGT |


| miR-26a-1-3p-rltm | CGCGCCTATTCTTGGTTACTT | GTGCAGGGTCCGAGGT |
| :---: | :---: | :---: |
| mir-130a-3p-rltm | GCGCCAGTGCAATGTTAA | GTGCAGGGTCCGAGGT |
| Clone primers |  |  |
| Primers for promoter cloning (PGL3-Basic) |  |  |
| Pitga1-1k | CGACGCGTGTGGCACCCTTCTCCTACTTTG | CCGCTCGAGGACGCCTGGGGGACCATTG |
| Pltga1-2k | CGACGCGTTGATGTTGGAGCAGTAGCTGAG | CCGCTCGAGGACGCCTGGGGACCATTG |
| Pitga1+1 | GGGGTACCGGGATTTGGTTCGTGAAGC | CCGCTCGAGGACGCCTGGGGACCATTG |
| Pitga1+100 | GGGGTACCCCCGCGAAGTTGGCTT | CCGCTCGAGGACGCCTGGGGACCATTG |
| Pitga1+200 | GGGGTACCATCCATCTGGGATCTGAGAAGC | CCGCTCGAGGACGCCTGGGGACCATTG |
| Pitga1+210 | GGGGTACCGATCTGAGAAGCGTGGAGC | CCGCTCGAGGACGCCTGGGGACCATTG |
| Pitga1+230 | GGGGTACCGGCTTAGCAGCATTCGACC | CCGCTCGAGGACGCCTGGGGACCATTG |
| Pitga1+250 | GGGGTACCAAACACAGGAAATTACTCTTCCACC | CCGCTCGAGGACGCCTGGGGACCATTG |
| Pitga1-Sp1mt | GTTTTGGTCGAATGCTGCTAATTTTTCTCCACGCTTCTCAGATCC | GGATCTGAGAAGCGTGGAGAAAAATTAGCAGCATTCG ACCAAAAC |
| Pitga1-Arntmt | GTGGAGCGGGCTTAGCAATATTGGACCAAAACACAGGAAATTACTCTTC | GAAGAGTAATTTCCTGTGTTTTGGTCCAATATTGCTA AGCCCGCTCCAC |
| Pitga1-Runx1mt | GGGCTTAGCAGCATTCGAGGACGACACAGGAAATTACTCTTCCACC | GGTGGAAGAGTAATTTCCTGTGTCGTCCTCGAATGCT GCTAAGCCC |
| Primers for 3'UTR cloning (pCl-neo) |  |  |
| Itga1 | GCTCTAGATTGGATTCTTCAAAAGGCCACTAAAG | AAGGAAAAAAGCGGCCGCCTGGCCAAACGGCTCTTCC |
| Itga1 148aMT | GCAGTTGAGCTTAAATTCTATGTAGAATAGCCTGACTAGATGGAGTCCTTATT TAAACATGAG | CTCATGTTTAAATAAGGACTCCATCTAGTCAGGCTAT TCTACATAGAATTTAAGCTCAACTGC |
| Itga1 181bMT | CAGATTGCTCCATTTCAATTACAATAACTAAATGTACGGTATCATCGTGTGTG A | TCACACACGATGATACCGTACATTTAGTTATTGTAAT TGAAATGGAGCAATCTG |
| Adcy9 | AAGGAAAAAAGCGGCCGCCTTTCACTGGTAAACTTCACTGTATAGC | AAGGAAAAAAGCGGCCGCGACTGCAGCCCAGGTGA |
| Adcy9 181bMT1 | TGTGACAATACCTCTTGCTTCTAAACATTCTGTTCCTGTACAATGCCACAGAT T | AATCTGTGGCATTGTACAGGAACAGAATGTTTAGAAG CAAGAGGTATTGTCACA |
| Adcy9 181bMT2 | GGCAGGAAGCAATACTTCAGAATTCATTCTGTGTAAATAGTTGCTTTGCATTG C | GCAATGCAAAGCAACTATTTACACAGAATGAATTCTG AAGTATTGCTTCCTGCC |
| Primers for gene expression (pLVXpuro) |  |  |
| Itga1 (mouse) | CCGCTCGAGATGGTCCCCAGGCGTC | GCTCTAGATCATTTCTCCATTTTCTTCTTTAGTG |
| Adcy9 (mouse) | CCGCTCGAGATGCAGTTACCTCTGTACCTGAGC | GCTCTAGATTAAGCGTAATCTGGAACATCGTATGGGT ACACACTCTTTGAGACATTGAGCTT |
| mir-218-2 | CCGCTCGAGACCTTGTCCCTCTTTGCTG | GCTCTAGAGTGGATACTCGAAGCACGG |
| let-7f-1 | CCGCTCGAGCATTTGCTTATGCTATGCATGC | GGAATTCCCAAAAGGCCTGGTCCTAG |
| miR-181b | CCGCTCGAGAAGCTCTGGGCTGGAGGA | GCTCTAGATTGAATAAACAAACCTGAAAGTTCAG |
| miR-181c | CCGCTCGAGTTTACATTATGGTTTGTATTTGTGCTG | GCTCTAGATTATTTCCCAATTCCAATCAGC |
| Primers for gene expression (pEGFP-C3) |  |  |
| Itga1 CDS | CCGCTCGAGATGGTCCCCAGGCGTC | GCTCTAGATCATTTCTCCATTTTCTTCTTTAGTG |
| Itga1 NC | CCGCTCGAGTAGGTCCCCAGGCGTC | GCTCTAGATCATTTCTCCATTTTCTTCTTTAGTG |
| Itga1 UTR | CCGCTCGAGATGGTCCCCAGGCGTC | GCTCTAGATCATTTCTCCATTTTCTTCTTTAGTG |
| ADCY9 UTR | CCGCTCGAGCTTTCACTGGTAAACTTCACTGTATAGC | GGAATTCGACTGCAGCCCAGGTGA |
| Primers for invitro trancription (pGEM-T) |  |  |
| Itga1 | TAATACGACTCACTATAGCTGGCTTCTCACCGTTATCC | AGGCATACAAGGGCCCAC |
| Adcy9 | TAATACGACTCACTATAGGGCCCTGCTTTCTGGC | GAAGAAATAATCTTTCATCAGGCTG |
|  |  |  |

