

**Supplementary data to:**

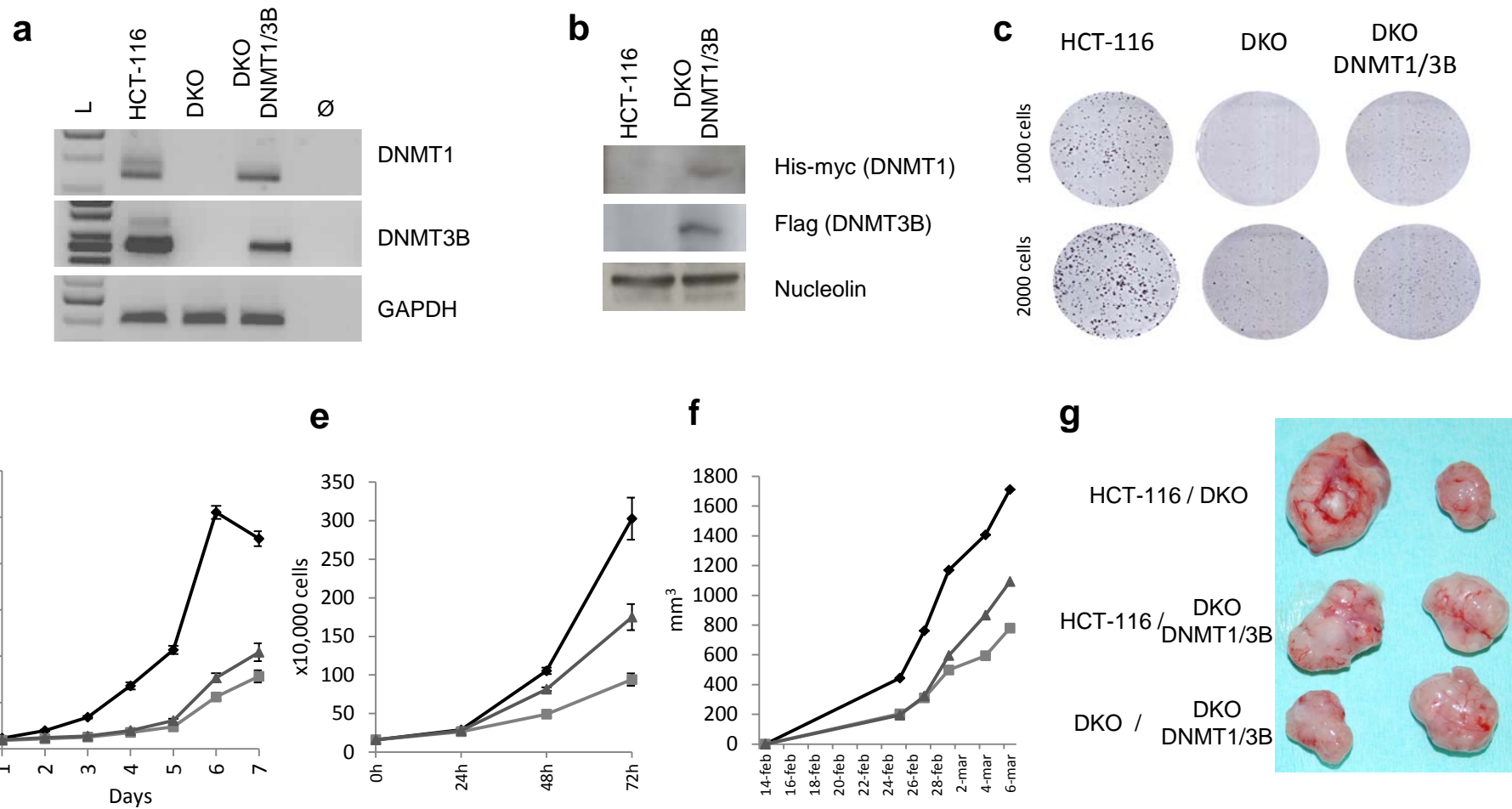
**DNA methylation determines nucleosome occupancy in the 5'-CpG islands of tumor suppressor genes**

Anna Portela, Julia Liz, Vanesa Nogales, Fernando Setién, Alberto Villanueva, Manel Esteller

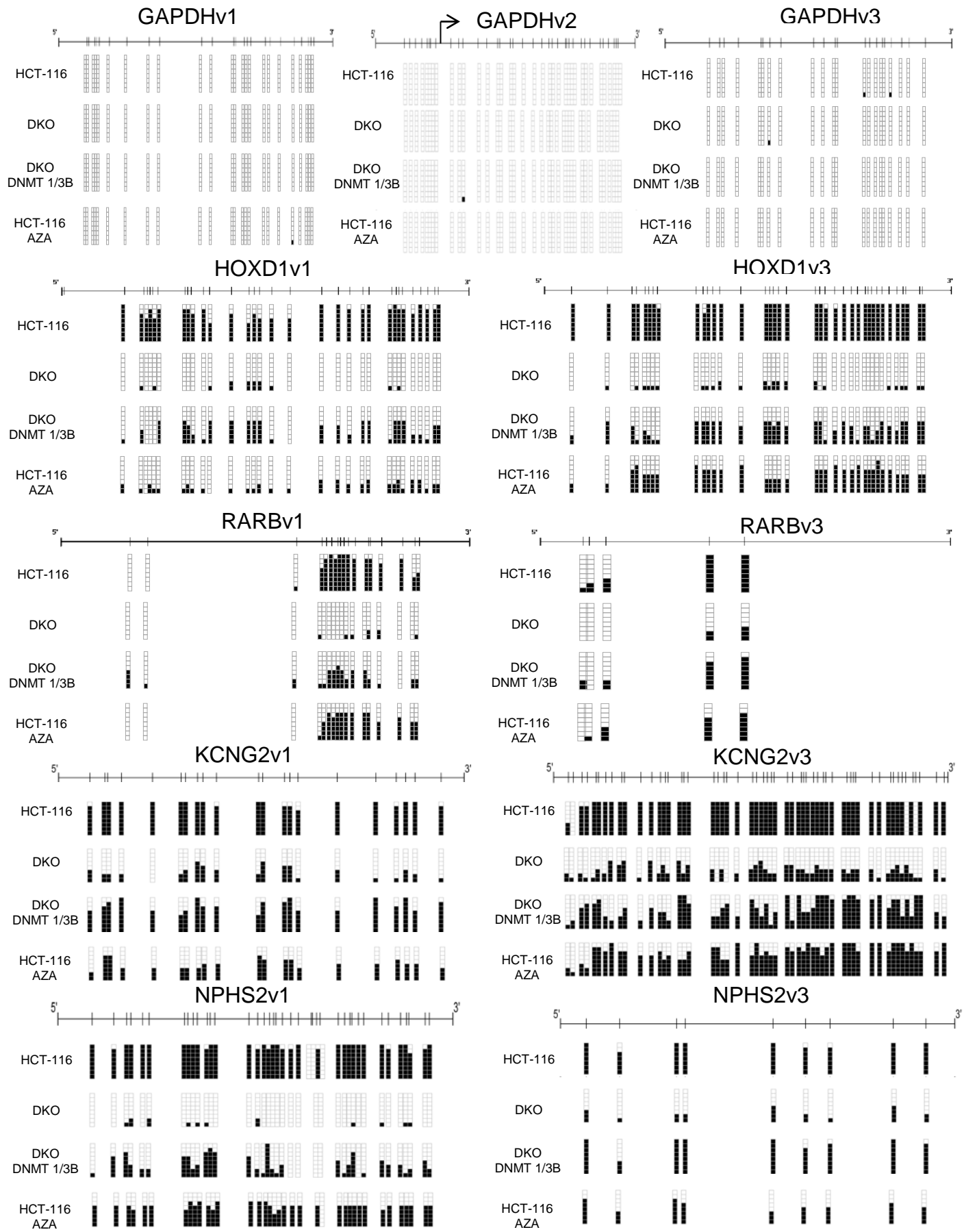
\* Supplementary Figures S1-S14

\* Supplementary Tables S1 & S2

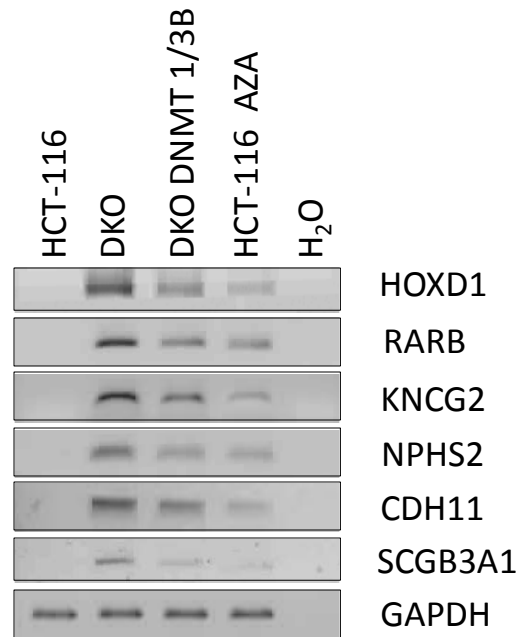
\* Supplementary Methods



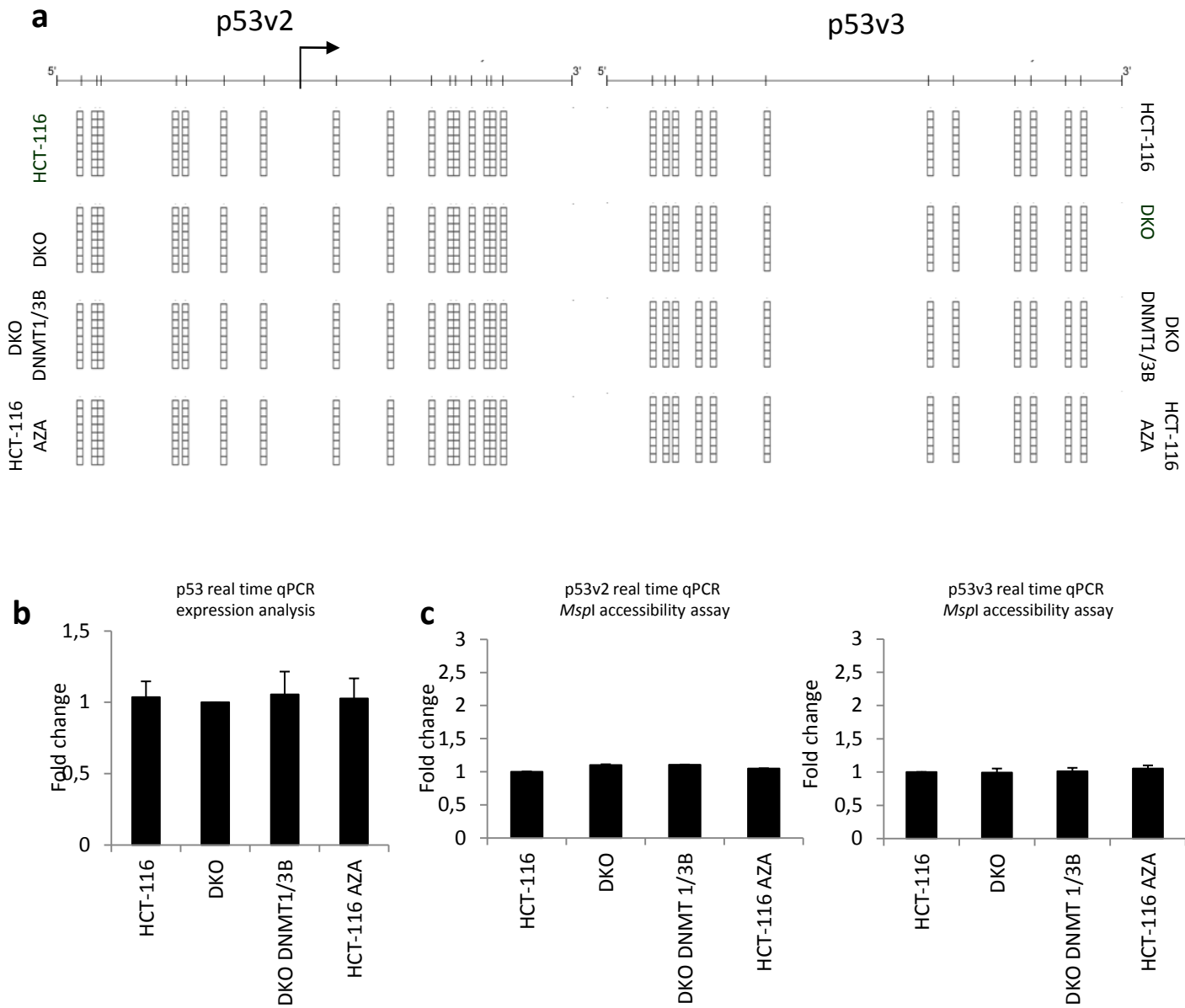
**Supplementary Figure S1.** Reintroduction of DNMT1 and DNMT3B into the DKO cell line. (a) RT-PCR in the DKO, DKO DNMT1/3B and HCT-116 cell line. *GAPDH* is used as a control. DNMT1 and DNMT3B are not present in the DKO cell line. In the HCT-116 cell lines different bands corresponding to different isoforms appear. However in the DKO DNMT1/3B just one band appears corresponding to the reintroduced isoform. Primers used are shown in Table I. L lane is the ladder. (b) Western blot in the DKO and DKO DNMT1/3B cell lines. Nucleolin was used as a control. Since the reintroduced DNMT1 and DNMT3B were marked with Flag and His-myc tags respectively, these antibodies were used in the Western. Again, DNMT1 and DNMT3B are present in the DKO DNMT1/3B cell line but not in the DKO. (c) Colony formation assay plating 1,000 cells and 2,000 cells. (d) Cell viability determined by the 3-(4, 5-dimethyl-2-thiazolyl)-2, 5-diphenyl-2H-tetrazolium bromide (MTT) assay. (e) Doubling time assay. The calculated doubling time is 14.95 hours for HCT-116, 26.01 hours for DKO and 19.92 hours for DKO DNMT1/3B. (f) In vivo nude mouse tumor-growth assay. Tumor volume were measured using digital calipers. Tumor volume (in mm<sup>3</sup>) was estimated according to the formula  $V = D \times d^2 / 2$ , where  $D$  is the long axis and  $d$  the short axis of tumor. Graphs (d), (e) and (f) legends: HCT-116 black rhombus, DKO light grey squares, and DKO DNMT1/3B dark grey triangles. (g) Representative tumors of nude mice 21 days after injection of  $3.5 \times 10^6$  cells.



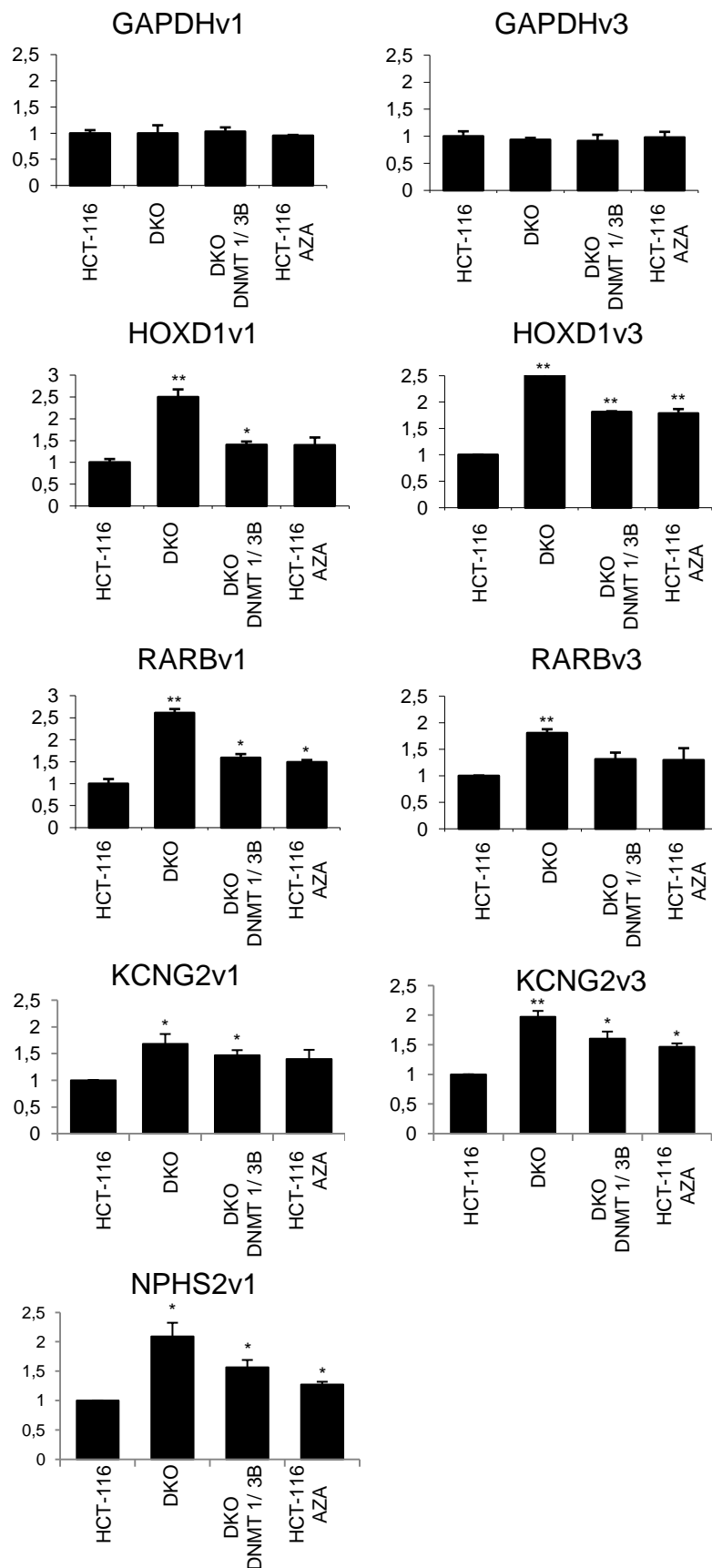
**Supplementary Figure S2.** DNA methylation patterns. Bisulfite sequencing of eight clones for each cell line/treatment studied. The regions presented in this figure are the ones not corresponding to the TSS, except for *GAPDH*. Region version 1 (v1) is the one located upstream the TSS, while version 3 (v3) is the one located downstream the TSS. White squares represent unmethylated CpG, while black ones represent methylated CpG.



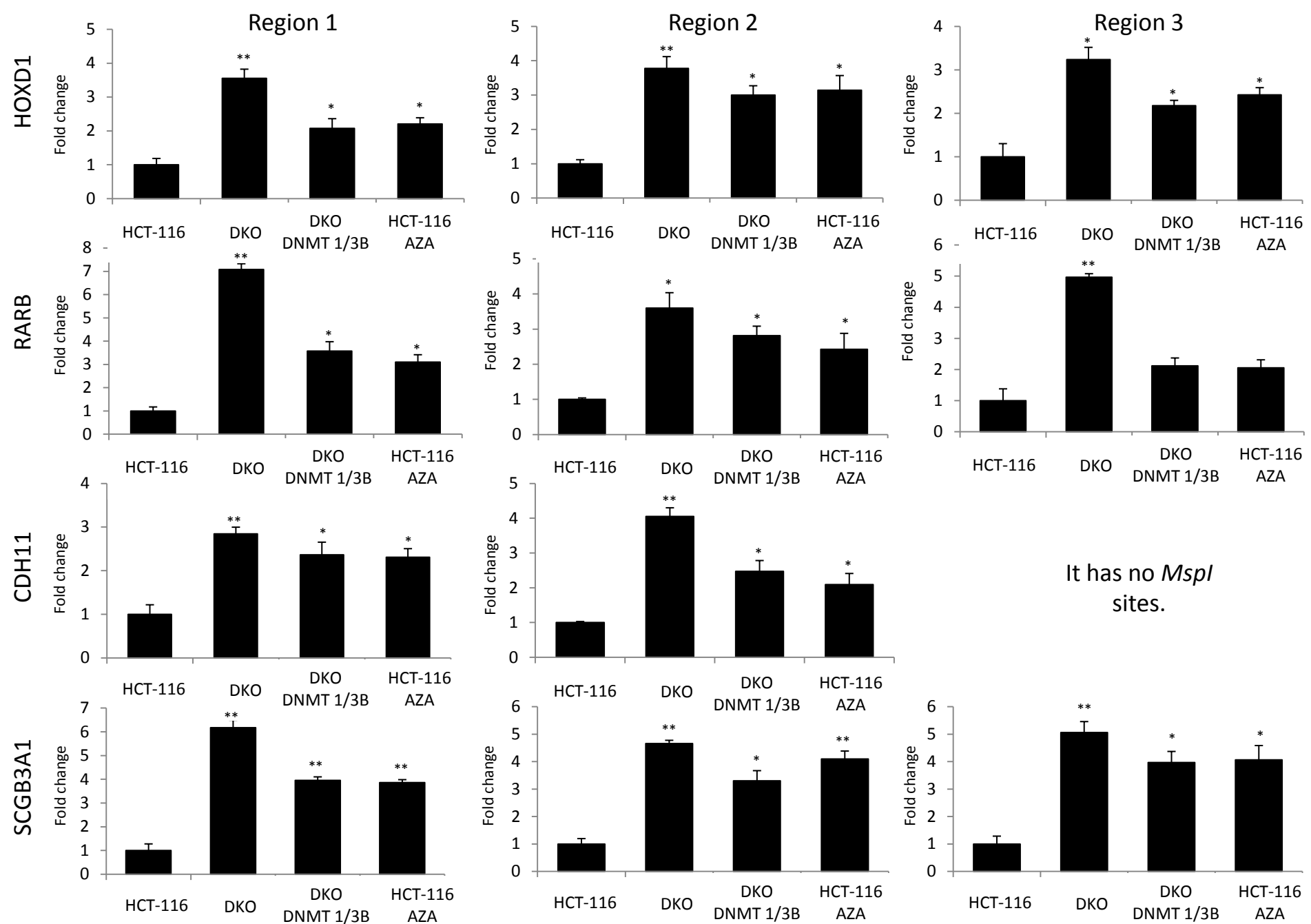
**Supplementary Figure S3.** Semi-quantitative PCR assessing gene expression. Expression of *HOXD1*, *RARB*, *KCNG2*, *NPHS2*, *CDH11* and *SCGB3A1* is shown for all the cell lines and cases studied. *GAPDH* expression, which is constitutive in all cell lines, was used as a control.



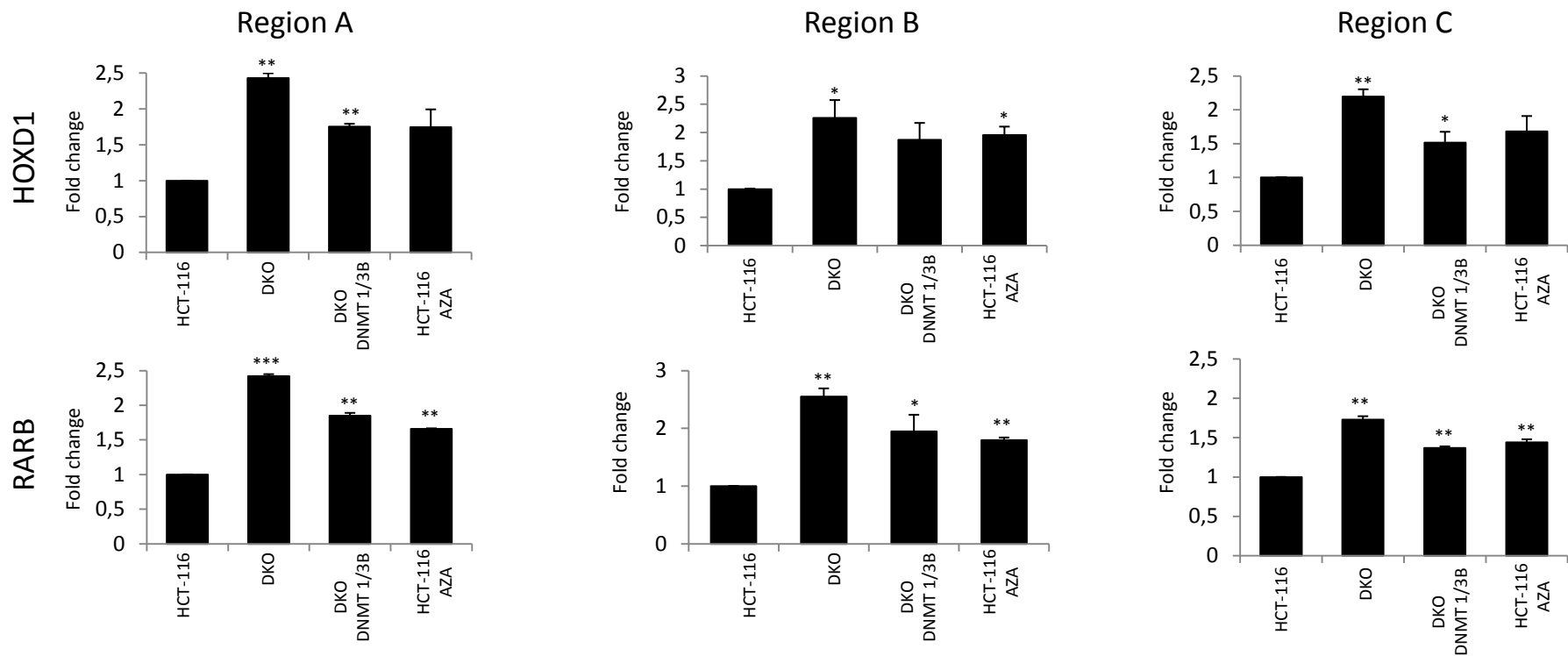
**Supplementary Figure S4.** *p53* gene promoter analysis for DNA methylation, RNA expression and nucleosome occupancy. (a) DNA methylation. Bisulfite sequencing of eight clones for each cell line/treatment studied. White squares represent unmethylated CpG, while black ones represent methylated CpG. (b) Gene expression. *GAPDH* expression, that is constitutive in all cell lines, was used to normalize the data. (c) *MspI* accessibility assay. The results are depicted as the fold change between undigested DNA and 400U/mL digested DNA.



**Supplementary Figure S5.** *MspI* accessibility assay. The results represent the ratio undigested/digested for each sample normalized to undigested/digested for HCT116 (\*  $p < 0.05$ , \*\*  $p < 0.01$ ). Thus, in the case of *GAPDH* they are 1 across all samples. Here the results from regions not containing the TSS are represented. Region version 1 (v1) is the one located upstream the TSS, while version 3 (v3) is the one located downstream the TSS. The results are similar to those obtained in the region containing the TSS: The accessibility is low in HCT-116 cells and much higher in DKO cells. When treating with Aza, HCT-116 becomes more accessible. When reintroducing DNMT1 and DNMT3B in DKO cells, they become less accessible.

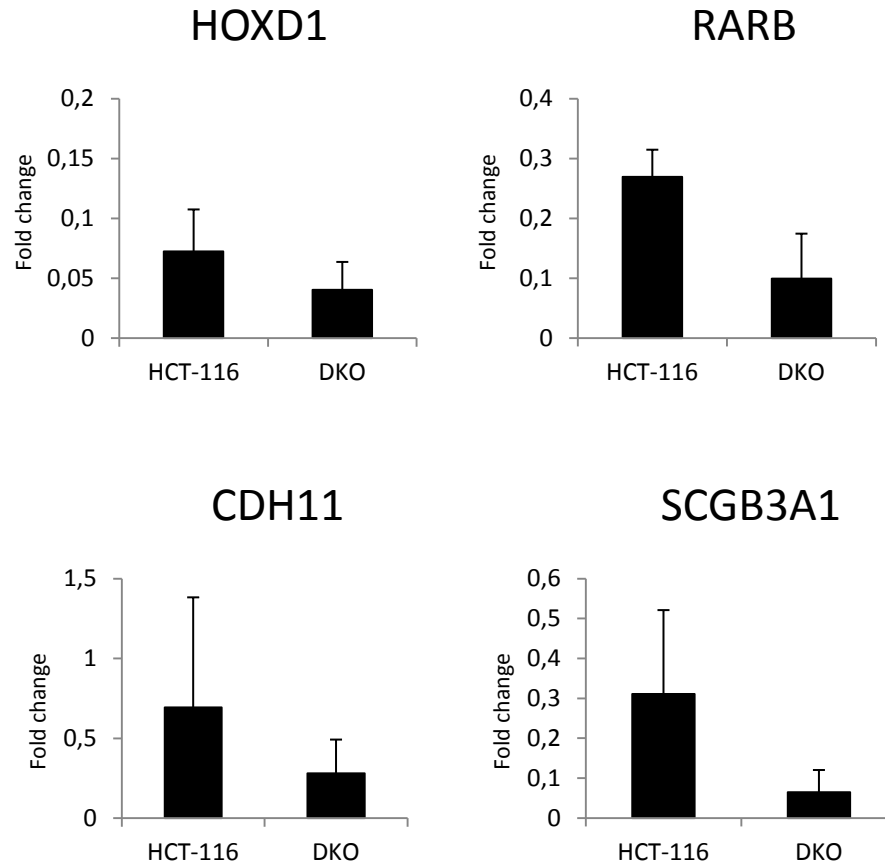


**Supplementary Figure S6.** *MspI* accessibility assay, 100U/mL results. The results are depicted as the fold change between undigested DNA versus 100U/mL digested DNA (\*  $p < 0.05$ , \*\*  $p < 0.01$ ). The accessibility is low in HCT-116 cells and much higher in DKO cells. When treating with the demethylating agent 5-aza-2'-deoxycytidine (Aza), HCT-116 becomes more accessible. When reintroducing DNMT1 and DNMT3B in DKO cells, they become less accessible. *MspI* accessibility assay directly correlates with nucleosome occupancy: higher accessibility, lower nucleosome occupancy.

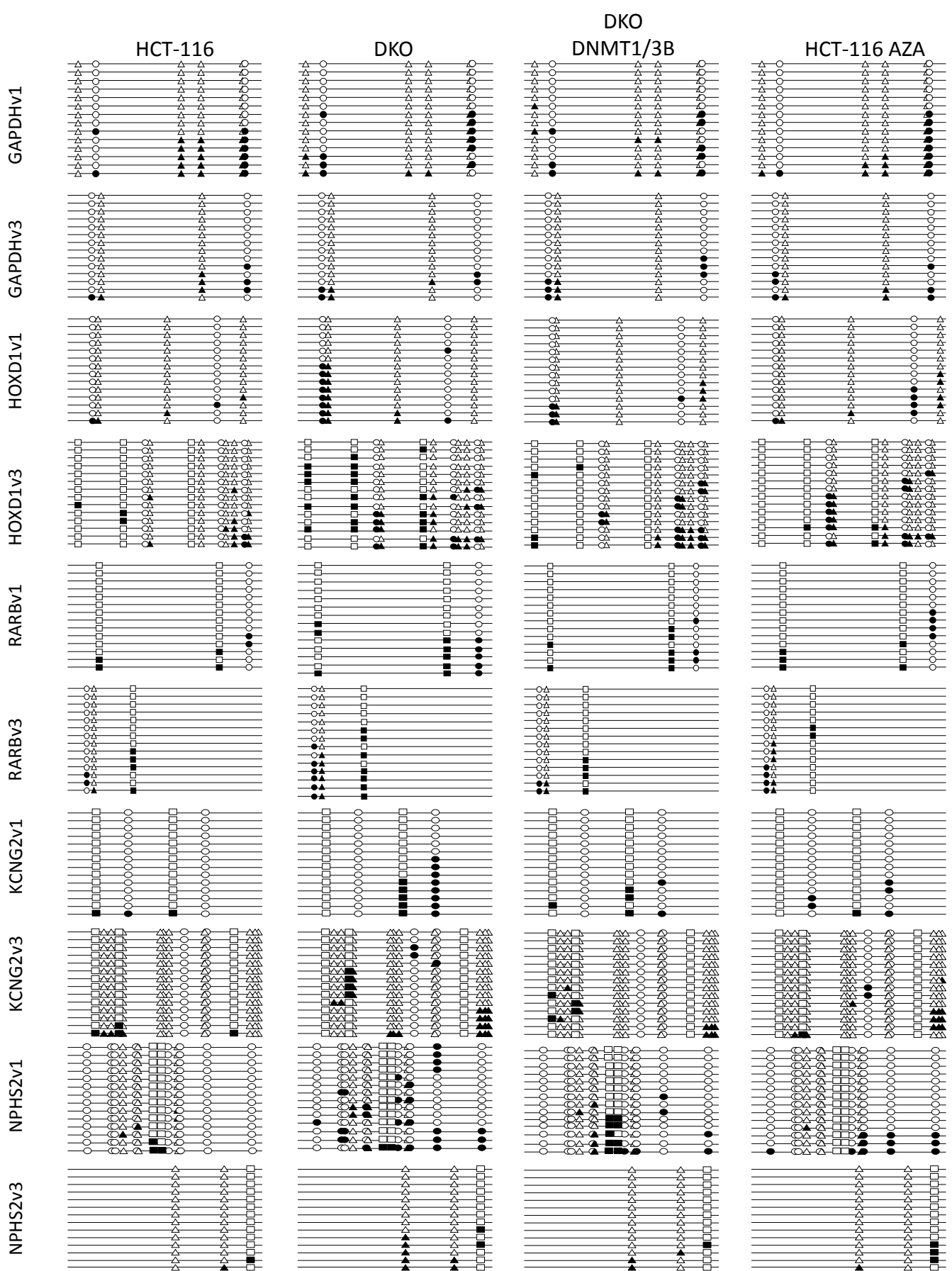


**Supplementary Figure S7.** *MspI* accessibility assay using additional primers to avoid a false positive if one primer is positioned in the linker of a nucleosome occupied region. The results are depicted as the fold change between undigested DNA and 400U/mL digested DNA (\*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$ ). The accessibility is low in HCT-116 cells and much higher in DKO cells. When treating with the demethylating agent 5-aza-2'-deoxycytidine (Aza), HCT-116 becomes more accessible. When reintroducing DNMT1 and DNMT3B in DKO cells, they become less accessible. *MspI* accessibility assay directly correlates with nucleosome occupancy: higher accessibility, lower nucleosome occupancy.

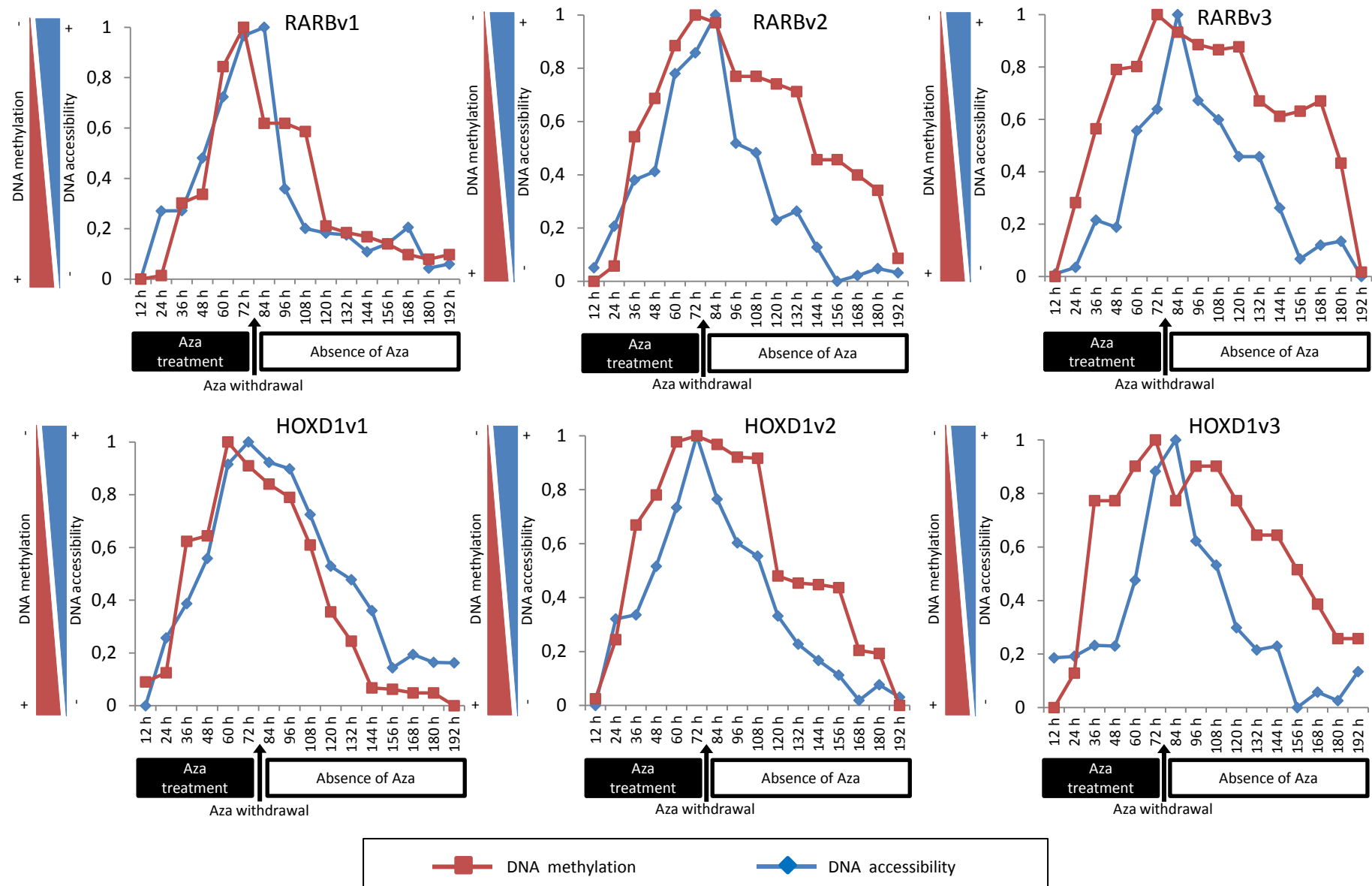




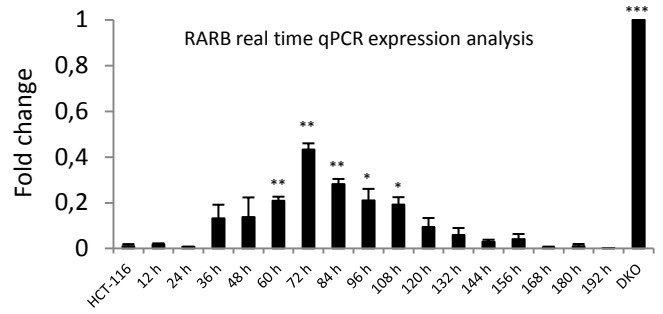
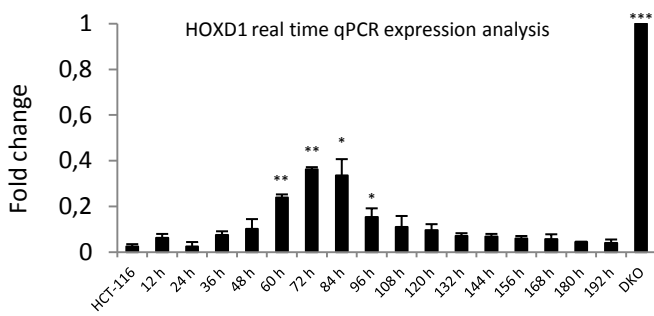
**Supplementary Figure S8.** Chromatin immunoprecipitation (ChIP) assay with H3 antibody performed on promoters regions of *HOXD1*, *RARB*, *CDH11* and *SCGB3A1* genes. Although no statistically significances are observed a clear tendency towards H3 depletion in active promoters can be observed.



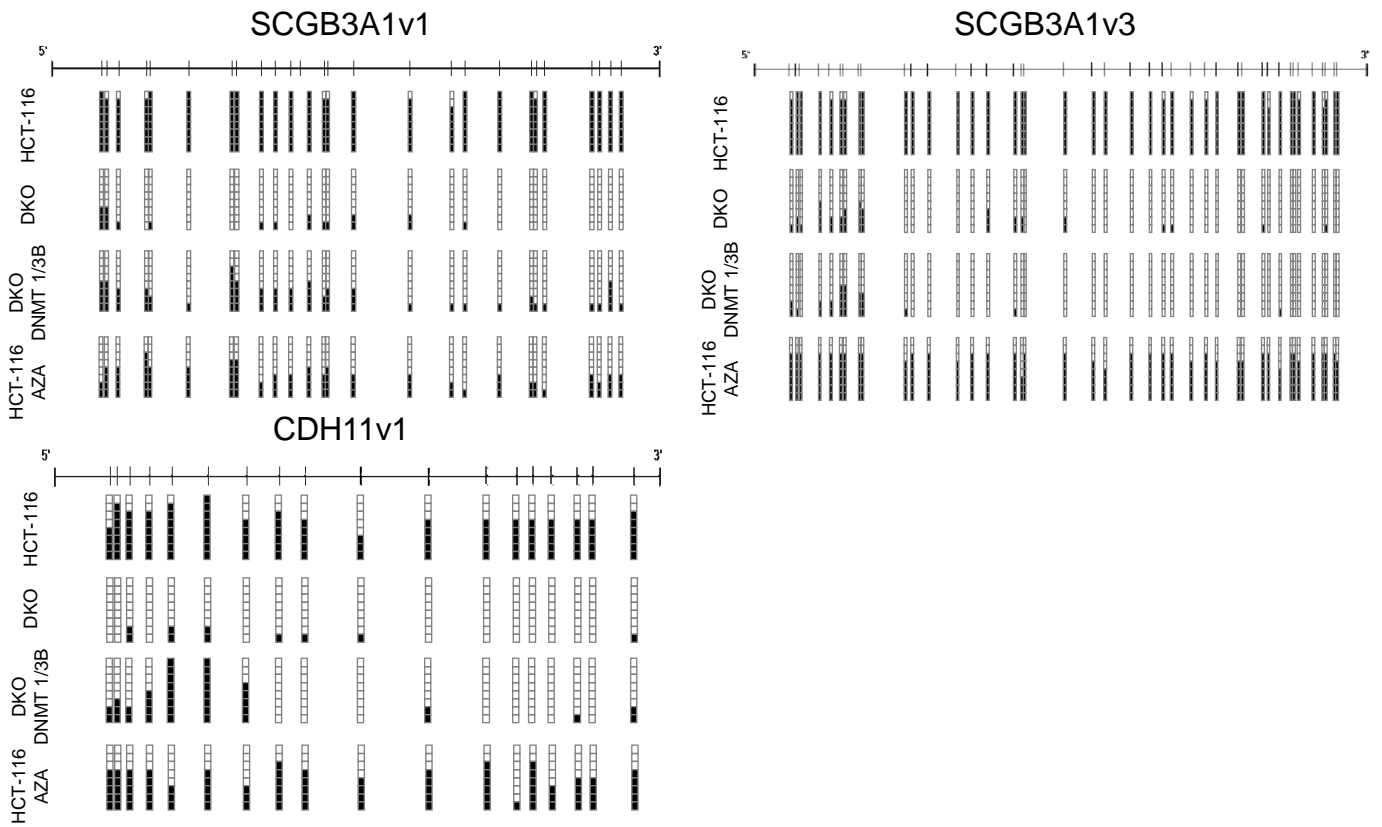
**Supplementary Figure S9.** M-SPA adapted protocol. Circles represent *MspI* methylation sites (C\*CGG), triangles represent *HaeIII* methylation sites (GGC\*C) and squares represent *AluI* methylation sites (AGC\*T). Black figures represent methylated sites, while white ones represent unmethylated. Version 1 (v1) corresponds to the region located upstream the TSS, while the version 3 (v3) corresponds to the region located downstream the TSS.



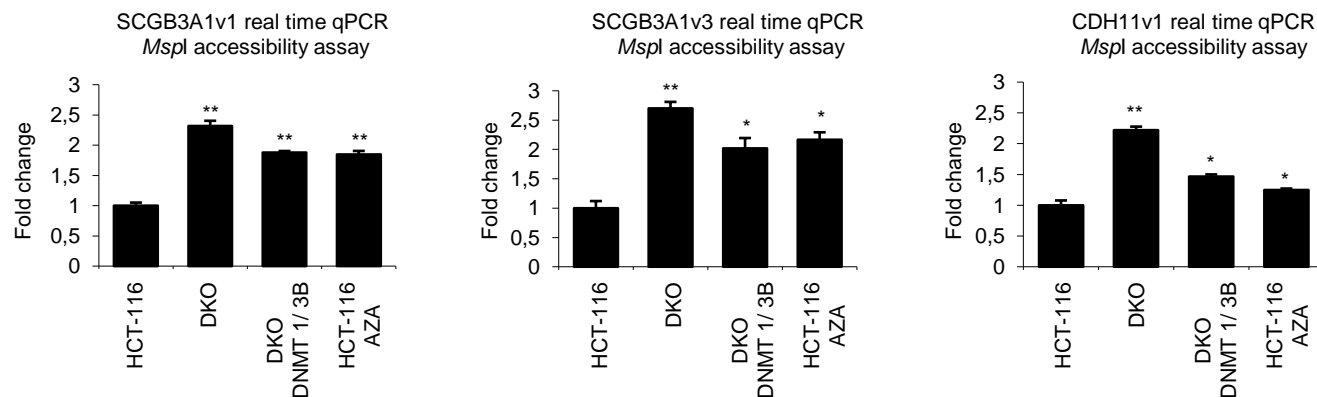
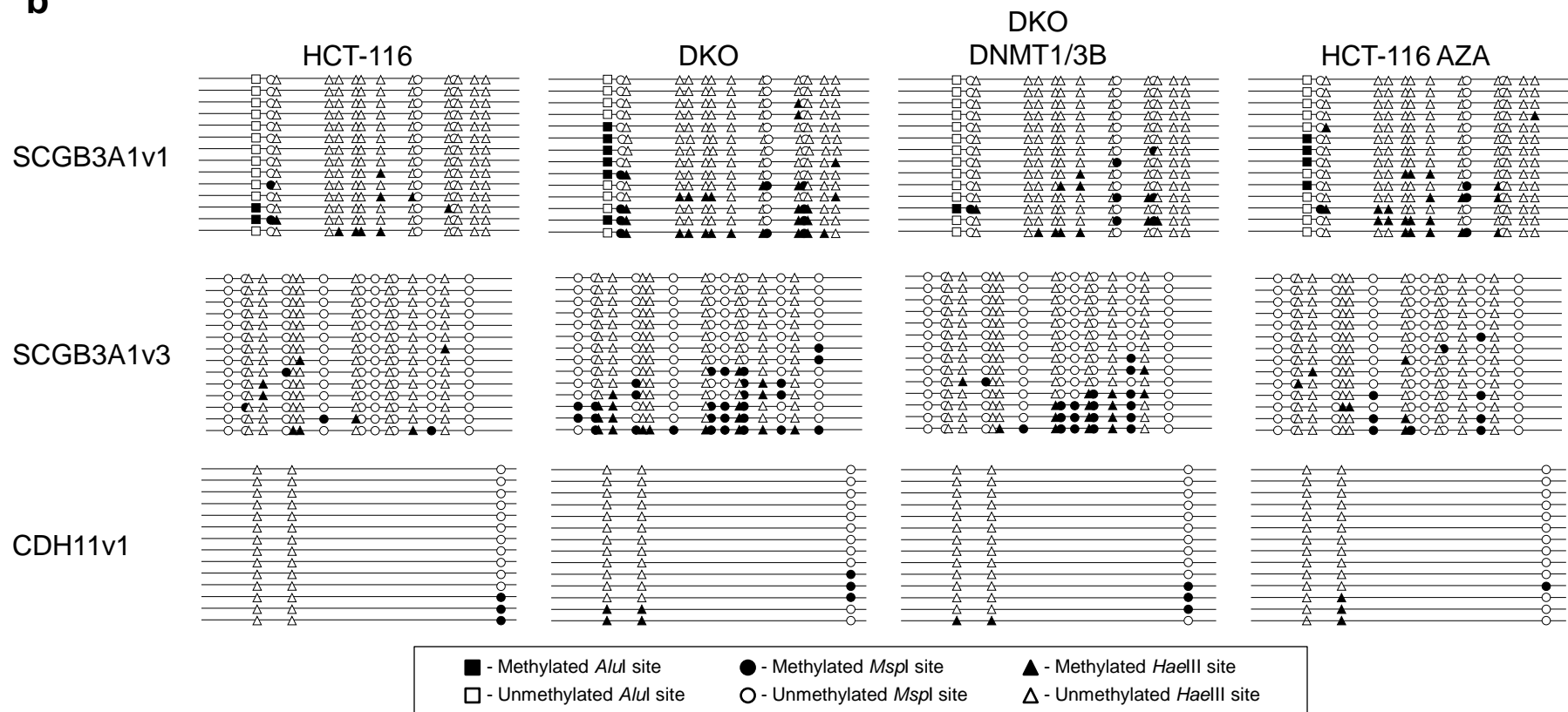
**Supplementary Figure S10.** Time course experiment for DNA methylation and DNA accessibility upon treatment of HCT-116 cells with the demethylating agent 5-aza-2'-deoxycytidine (Aza). The graphs shows sixteen different time points (until 192 hours): six time points with continuous Aza treatment and ten time points after Aza withdrawal at 72 hours. Every 12 hours DNA methylation bisulfite genomic sequencing analysis and *MspI* accessibility assays for three regions of the *HOXD1* and *RARB* promoter CpG islands were performed. Cells were never allowed to reach confluence. DNA methylation data and *MspI* accessibility assays data have been plotted in a single graph in order to facilitate interpretation. Absolute value of 1 in DNA methylation represents the maximum demethylation percentage achieved with the Aza treatment after analyzing eight bisulfite sequencing clones. Absolute value of 1 in DNA accessibility represents the maximum DNA accessibility achieved with the Aza treatment analyzed by *MspI* accessibility assay. The Y axis of the graphs depicts these absolute scaled values.



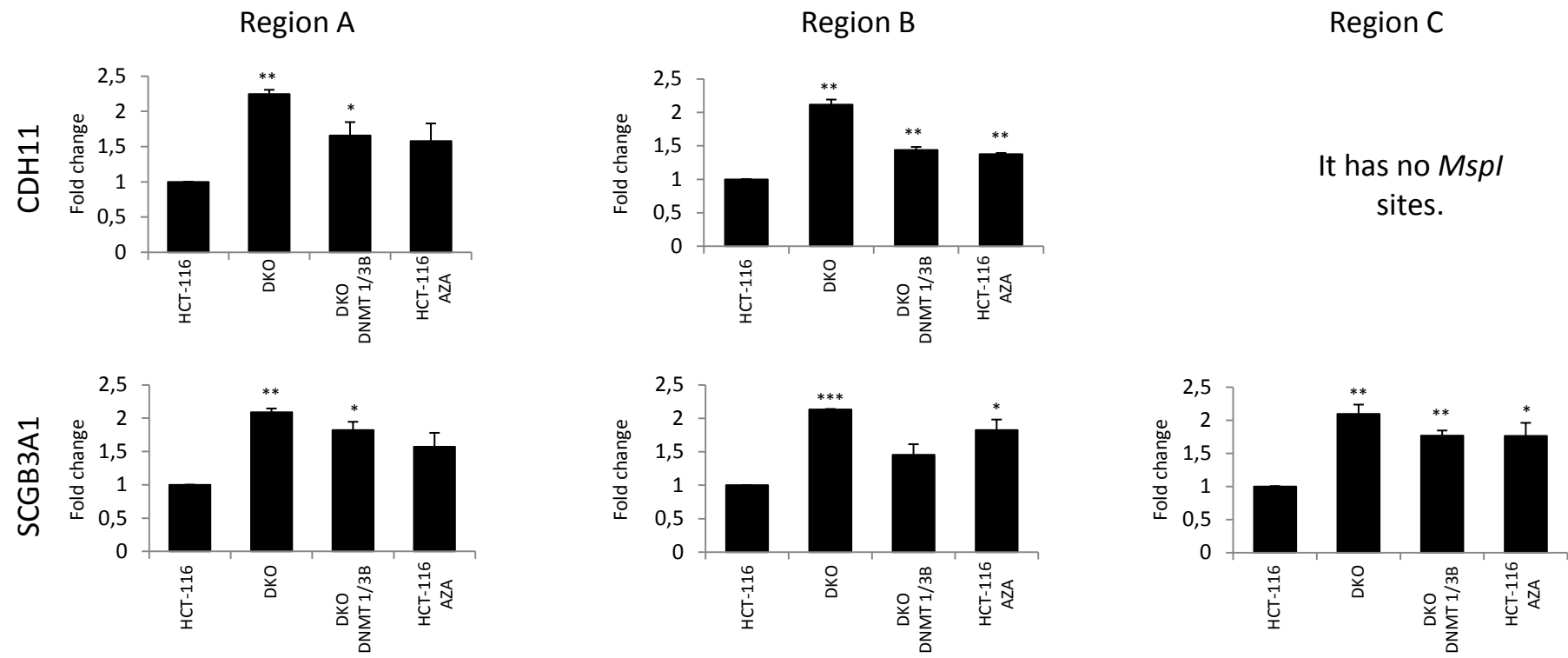
**Supplementary Figure S11.** Time course experiment for gene expression upon treatment of HCT-116 cells with the demethylating agent 5-aza-2'-deoxycytidine (Aza). *GAPDH* expression, was used to normalize the data. (\*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$ ).



**Supplementary Figure S12.** DNA methylation patterns. Bisulfite sequencing of eight clones for each cell line/treatment studied. The regions presented in this figure are the ones not corresponding to the TSS. Region version 1 (v1) is the one located upstream the TSS, while version 3 (v3) is the one located downstream the TSS. White squares represent unmethylated CpG, while black ones represent methylated CpG.

**a****b**

**Supplementary Figure S13.** (a) *MspI* accessibility assay. The results are depicted as the fold change between undigested DNA and 400U/mL digested DNA (\*  $p < 0.05$ , \*\*  $p < 0.01$ ). Here the results from regions not containing the TSS are represented. Region version 1 (v1) is the one located upstream the TSS, while version 3 (v3) is the one located downstream the TSS. (b) M-SPA adapted protocol. Circles represent *MspI* methylation sites (C\*CGG), triangles represent *HaeIII* methylation sites (GGC\*C) and squares represent *AluI* methylation sites (AGC\*T). Black figures represent methylated sites, while white ones represent unmethylated. Version 1 (v1) corresponds to the region located upstream the TSS, while the version 3 (v3) corresponds to the region located downstream the TSS. Accessible regions, where nucleosomes are not positioned become methylated, while inaccessible not.



**Supplementary Figure S14.** *MspI* accessibility assay using additional primers to avoid a false positive if one primer is positioned in the linker of a nucleosome occupied region. The results are depicted as the fold change between undigested DNA and 400U/mL digested DNA (\* p<0.05, \*\* p<0.01, \*\*\* p<0.001). The accessibility is low in HCT-116 cells and much higher in DKO cells. When treating with the demethylating agent 5-aza-2'-deoxycytidine (Aza), HCT-116 becomes more accessible. When reintroducing DNMT1 and DNMT3B in DKO cells, they become less accessible. *MspI* accessibility assay directly correlates with nucleosome occupancy: higher accessibility, lower nucleosome occupancy.

### Supplementary Table S1. Primer sequences

#### Primers for bisulfite genomic sequencing and adapted M-SPA:

Primer name	Orientation	Sequence	TSS distance	Amplicon size
BS-GAPDHv1_s	Sense	TTAGTTTTTGAAAGAAAAGAAAGG	-431	361bp
BS-GAPDHv1_a	Antisense	CCCAAATCTTAAAACCTAAAC	-70	
BS-GAPDHv2_s	Sense	GTTTTAAGATTTTGGGTTGGGA	-86	334bp
BS-GAPDHv2_a	Antisense	ACCAAACCTCCATACCCAAC	+248	
BS-GAPDHv3_s	Sense	GTTGGGTATGGAGGTTTGGT	+228	255bp
BS-GAPDHv3_a	Antisense	AAAACAACCTACCCTACCCCAT	+483	
BS-HOXD1v1_s	Sense	GYGTAGAGGATTTAGAAGAGGGGA	-405	370bp
BS-HOXD1v1_a	Antisense	ACCAAATTAACCAAAAACAACC	-35	
BS-HOXD1v2_s	Sense	TTGTTTTGGTTAATTTGGTT	-54	269bp
BS-HOXD1v2_a	Antisense	CCCCACCTTTCTAAAAAC	+215	
BS-HOXD1v3_s	Sense	TTTTAGAAAGGTGGGGTT	+199	293bp
BS-HOXD1v3_a	Antisense	ACCCCTCCAAAATACAC	+492	
BS-RARBv1_s	Sense	GTGTGTTTGGGATAGGGGTAATT	-722	518bp
BS-RARBv1_a	Antisense	CTTTCCTATTTCTCTCTTAAAAAC	-204	
BS-RARBv2_s	Sense	GGGTTGTTGGGAGTTTTTAAGT	-151	367bp
BS-RARBv2_a	Antisense	CAAAAAATCCCAAATTCTCCT	+216	
BS-RARBv3_s	Sense	AAGGAGAATTTGGGATTTTTTT	+193	322bp
BS-RARBv3_a	Antisense	AAATCCAAAATTTACCCAAAAC	+515	
BS-KCNG2v1_s	Sense	TAGTTTTTTGGTTGATTTTGA	-491	302bp
BS-KCNG2v1_a	Antisense	CCCRACCTCTACACCTAATC	-189	
BS-KCNG2v2_s	Sense	GGAGGGGTTTTYGAGYTTAT	-161	264bp
BS-KCNG2v2_a	Antisense	ACRCRCCCATACCAAAC	+103	
BS-KCNG2v3_s	Sense	GAGTTTTTTTTYGATYGTAGT	+200	402bp
BS-KCNG2v3_a	Antisense	CCCRAATACRAATTATCCAC	+602	
BS-NPHS2v1_s	Sense	GGAATTTTTTAGGAGATGAGTTTT	-565	368bp
BS-NPHS2v1_a	Antisense	CCTCTCCATCCTCAAARCTAC	-197	
BS-NPHS2v2_s	Sense	GTAGYTTTGAGGATGGAGAGG	-218	366bp
BS-NPHS2v2_a	Antisense	AAAAATAACCTTTCCACCTTA	+148	
BS-NPHS2v3_s	Sense	TTTTAGGTTGTAATTAAGGGG	+97	354bp
BS-NPHS2v3_a	Antisense	AACCTACAACCTACAACCACC	+451	
BS-CDH11v1_s	Sense	TAGGGGTTAGTATTTTTGGG	-284	224bp
BS-CDH11v1_a	Antisense	ACRCRCTAATAACAAAAAT	-60	
BS-CDH11v2_s	Sense	TTTTATTTTTGTTATTAGYGYG	-84	213bp
BS-CDH11v2_a	Antisense	TAAACRCAACCTCCRAAC	+129	
BS-SCGB3A1v1_s	Sense	TAGGGATTAGGGAGTTAGGAAT	-390	311bp
BS-SCGB3A1v1_a	Antisense	CTCCTAAAAAACCCCTACCC	-79	
BS-SCGB3A1v2_s	Sense	GGGTAGGGTTTTTTTAGGAG	-99	279bp
BS-SCGB3A1v2_a	Antisense	AAAAAATCAACTAAAATCCACRAT	+180	
BS-SCGB3A1v3_s	Sense	ATYGTGGATTTTAGGTTTTTT	+156	451bp
BS-SCGB3A1v3_a	Antisense	CCCCAAAAACAATCCA	+607	
BS-p53v2_s	Sense	AAAATGTTAGTATTTAYGGTATTAGGT	-160	363bp
BS-p53v2_a	Antisense	AAAAAAAACCTCATCAAATCAA	+203	
BS-p53v3_s	Sense	TTGAATTTGATGAGTTTTTTTTG	+181	324bp
BS-p53v3_a	Antisense	CATCTTTTATTTCAAAAATTCCC	+505	

#### Primers for quantitative real time PCR:

Primer name	Orientation	Sequence	Amplicon size
qPCR-GAPDH_s	Sense	TCTTCTTTTGCGTCGCCAG	372bp
qPCR-GAPDH_a	Antisense	AGCCCCAGCCTTCTCCA	
qPCR-HOXD1_s	Sense	TTTTCCGGCTTGCTCAAAG	318bp
qPCR-HOXD1_a	Antisense	AGGTGCAAGCAGTTGGCTAT	
qPCR-RARB_s	Sense	TGCCAATACTGTGCGACTCCA	195bp
qPCR-RARB_a	Antisense	CTGGCAGAGTGAAGGGAAAG	
qPCR-KCNG2_s	Sense	CCTCTGCCTGAGACCCAT	225 bp
qPCR-KCNG2_a	Antisense	AGCAGCAGCGACACGTAGA	
qPCR-NPHS2_s	Sense	CTGCGTAAAGGTTGTACAAGAG	277 bp
qPCR-NPHS2_a	Antisense	TGCACAGCTTTAGATACATGAG	



qPCR-CDH11_s	Sense	GTTCTTGGCCCCAAGTTACA	314bp
qPCR-CDH11_a	Antisense	TGGGAGCATTATCGTTGACA	
qPCR- SCGB3A1_s	Sense	CCGTGAACCACCTCATAGAG	237bp
qPCR- SCGB3A1_a	Antisense	TTAACCACGTTTATTGAGAGGG	
qPCR- p53_s	Sense	CTCAGATAGCGATGGTCTGG	285bp
qPCR- p53_a	Antisense	CAACTGTGCAATAGTTAAACCC	

**Primers for *MspI* accessibility assay:**

Primer name	Orientation	Sequence	TSS distance	Amplicon size
MspI-GAPDHv1_s	Sense	CTCAGTCGTTCCCAAAGTCC	-349	273bp
MspI-GAPDHv1_a	Antisense	GTCTTGAGGCCTGAGCTACG	-76	
MspI-GAPDHv2_s	Sense	CGTAGCTCAGGCCTCAAGAC	-96	209bp
MspI-GAPDHv2_a	Antisense	CTAGCCTCCCGGGTTTCTCT	+113	
MspI-GAPDHv3_s	Sense	AGAGAAACCCGGGAGGCTA	+93	274bp
MspI-GAPDHv3_a	Antisense	TGACTCCGACCTTCACCTTC	+367	
MspI-HOXD1v1_s	Sense	AAGCGCAGAGGACTCAGAAG	-407	262bp
MspI-HOXD1v1_a	Antisense	CCTGCTCTCGGACAGGTATT	-145	
MspI-HOXD1v2_s	Sense	ACCTGCCCAATACCTGT	-147	232bp
MspI-HOXD1v2_a	Antisense	GAGCCGGAGTAAATAGTGG	+85	
MspI-HOXD1v3_s	Sense	CAGTCTGCTCAGCCTCTG	+149	359bp
MspI-HOXD1v3_a	Antisense	GGCACCAGTTTCGTAGGC	+508	
MspI-RARBv1_s	Sense	AAGGCGCACAGAGGAATTTA	-429	274bp
MspI-RARBv1_a	Antisense	AAAGCAGACAGCCAGAGAGG	-155	
MspI-RARBv2_s	Sense	CCTCTCTGGCTGTCTGCTTT	-175	271bp
MspI-RARBv2_a	Antisense	TCCAGTCCTCAAACAGCTC	+96	
MspI-RARBv3_s	Sense	GCTGTTTGAGGACTGGGATG	+78	279bp
MspI-RARBv3_a	Antisense	GCACGTAGGCTGTTGGTCTT	+357	
MspI-KCNG2v1_s	Sense	GGGACACACCGTGAGAACTA	-455	204bp
MspI-KCNG2v1_a	Antisense	GTGACCCGCTTGAGTTATC	-251	
MspI-KCNG2v2_s	Sense	GGGTCTCCGAGCTCACCT	-157	228bp
MspI-KCNG2v2_a	Antisense	CCCACGTTGATGATGACG	+71	
MspI-KCNG2v3_s	Sense	CGACGAGCTGGCCTACTG	+305	209bp
MspI-KCNG2v3_a	Antisense	AGTGCGGGTTGTCCACCA	+514	
MspI-NPHS2v1_s	Sense	CAGGCCTCTCTGCTTCAG	-468	206bp
MspI-NPHS2v1_a	Antisense	GCAGTCCCTGTGGAGTCG	-262	
MspI-NPHS2v2_s	Sense	GGAGAACAAGAGGGCAAAGG	-141	327bp
MspI-NPHS2v2_a	Antisense	AGCATCCAGCAATCTGCTCT	+186	
MspI-HOXD1vA_s	Sense	TCTAGGAAAGGGGGAAGAA	-491	189bp
MspI-HOXD1vA_a	Antisense	AAGGTTAAATGGGAGCGTGA	-302	
MspI-HOXD1vB_s	Sense	GGGCTGCTTTGGCTAACTT	-57	191bp
MspI-HOXD1vB_a	Antisense	CTCCGCCAGCCCTCTCTAC	+134	
MspI-HOXD1vC_s	Sense	GCCTTCGTGCTGCTGTCTGC	+364	208bp
MspI-HOXD1vC_a	Antisense	AGTCGTACGCCGGCCCGGA	+572	
MspI-RARBvA_s	Sense	TGCATGTGCTTTTTCTGGAG	-488	294bp
MspI-RARBvA_a	Antisense	CCGGCGTTTTCTTTCCTATT	-194	
MspI-RARBvB_s	Sense	TGGGAGTTGGTGATGTCAGA	-116	258bp
MspI-RARBvB_a	Antisense	GACGGTGCCCAGACAAAC	+142	
MspI-RARBvC_s	Sense	ATCCGAGCAGGGTTTGTCT	+113	301bp
MspI-RARBvC_a	Antisense	GGAGGCAAATGGCATAGAAA	+414	
MspI-CDH11v1_s	Sense	TCCAGGGGTTAGCATCTCTG	-284	224bp
MspI-CDH11v1_a	Antisense	CGCTAGTGGCAGGAATGAG	-60	
MspI-CDH11v2_s	Sense	GGTTTCTCATTCTGCCACT	-84	213bp
MspI-CDH11v2_a	Antisense	CTTGAGGGTGGACGCAAC	+129	
MspI-SCGB3A1v1_s	Sense	CACGGTCTGGGATCAGAGG	-409	291bp
MspI-SCGB3A1v1_a	Antisense	CCTGGCCAACCTTCCTGCT	-118	
MspI-SCGB3A1v2_s	Sense	GGCAGGGCTTTCAGGA	-98	273bp
MspI-SCGB3A1v2_a	Antisense	AGGACCTGGGATCCACGA	+175	
MspI-SCGB3A1v3_s	Sense	GGATCCCAGGTCTCCAG	+161	211bp
MspI-SCGB3A1v3_a	Antisense	CAAGGGAGGGGACACTCG	+372	
MspI-CDH11vA_s	Sense	CCAATTCAGTCGCTCCAG	-366	307bp
MspI-CDH11vA_a	Antisense	GCGCTAGTGGCAGGAATG	-59	
MspI-CDH11vB_s	Sense	GGACGGTGGTATCTGAGTCG	+244	224bp
MspI-CDH11vB_a	Antisense	CTCTGCCCCAGCCAGGTA	+468	

Mspl-SCGB3A1vA_s	Sense	AAAAACGCCCACTTCTGTT	-552	282bp
Mspl-SCGB3A1vA_a	Antisense	ACCTTCGCTTTGCGGTCT	-270	
Mspl-SCGB3A1vB_s	Sense	TCCTGCAGCTCCGGTGAG	+63	202bp
Mspl-SCGB3A1vB_a	Antisense	GCTGGAGACAGCCCTGAG	+265	
Mspl-SCGB3A1vC_s	Sense	CTCAGGGCTGTCTCCAGC	+247	248bp
Mspl-SCGB3A1vC_a	Antisense	AGCCCCGGGACACAGGCGGG	+495	
Mspl-p53v2_s	Sense	CTCCCCAACTCCATTTCCCTT	-106	286bp
Mspl-p53v2_a	Antisense	CAGGAGCTTACCCAATCCAG	+180	
Mspl-p53v3_s	Sense	GTGGGGACTTAGCGAGTTTG	+269	254bp
Mspl-p53v3_a	Antisense	CCTCAATGCTTTGTGCATCT	+523	
Mspl-Neg_s	Sense	TTGATTATAGGGGGCAGTCTG	+4375	200bp
Mspl-Neg_a	Antisense	AAGGTCTTGGGCAATGT	+4575	

### Primers for RT-PCR:

Primer name	Orientation	Sequence	Amplicon size
qPCR-GAPDH_s	Sense	TCTTCTTTTGGCTCGCCAG	372bp
qPCR-GAPDH_a	Antisense	AGCCCCAGCCTTCTCCA	
RT-PCR_DNMT1_s	Sense	GCACGAATTTCTGCAAACAG	328-376bp
RT-PCR_DNMT1_a	Antisense	TGTAATCCTGGGGCTAGGTG	
RT-PCR_DNMT3B_s	Sense	GGAGACTCATTGGAGACCA	252-312bp
RT-PCR_DNMT3B_a	Antisense	GGCAACATCTGAAGCCATTT	

### Primers for CHIP:

Primer name	Orientation	Sequence	TSS distance	Amplicon size
ChIP_HOXD1_s	Sense	GGGCTGCTTTGGCTAACTT	-57	147bp
ChIP_HOXD1_a	Antisense	CGAGTGAGCCGGAGGTAAAT	+90	
ChIP_RARB_s	Sense	TGGGAGTTGGTGATGTCAGA	-116	147bp
ChIP_RARB_a	Antisense	CTGCCTCTGAACAGCTCACTT	+31	
ChIP_CDH11_s	Sense	CCCCGGTTTCTCATTCTT	-88	143bp
ChIP_CDH11_a	Antisense	AGTCCCAGTCCCATTAC	+55	
ChIP_SCGB3A1_s	Sense	GGGCGAGACCGGGTATAAG	-56	135bp
ChIP_SCGB3A1_a	Antisense	CACCGGAGCTGCAGGACA	+79	
ChIP_GAPDH_s	Sense	GGGCTGGGACTGGCTGAG	-73	152bp
ChIP_GAPDH_a	Antisense	CTGGCGACGCAAAAAGAAG	+79	

**Supplementary Table S2**

TargetID	Prob eID	HCT116-MONO.AVG Beta	HCT116.AVG Beta	HCT116-DKO.AVG Beta	PROBE_ID	GID	ACCESSIO N	SYMBOL	GEN E_ID	CHRO M.	CPG _COORDI NATE	DIST_ TO_TS S	CPG ISLAND	INPUT_SEQUENCE	CG_NO
AATK_P519_R	3	0.96097	0.96569	0.07763	AATK_P519_R	8.9E+07	XM_927215.1	AATK	9625	17	76710413	-519	Y	GGGGACGTGCCAGTGGGTCT[CG]AAGAAGGCAGGACAGAAGGCCGG	cg17279079
AATK_P709_R	10	0.9576	0.88532	0.03098	AATK_P709_R	8.9E+07	XM_927215.1	AATK	9625	17	76710603	-709	Y	ACGGGTGCCCCGTGGCCAGCAG[CG]GCTCCATGGCCAGCGAGGCCGG	cg02979355
ADAMTS12_E52_R	2989	0.9442	0.92857	0.04124	ADAMTS12_E52_R	5.2E+07	NM_030955.2	ADAMTS12	81792	5	33927829	52	Y	AGATGCAGGGTGCATGGTCAGGCG[CG]AGAAGGCAGCGACTGCAAGCTGCC	cg13887940
CCKBR_P480_F	1753	0.90564	0.92422	0.05106	ADAMTS12_P250_R	5.2E+07	NM_030955.2	ADAMTS12	81792	5	33928131	-250	Y	CGAACGCCAGGCCAGCTGCCGAGC[CG]GCCAAATAGGGGAGACCCGG	cg24560027
ADCYAP1_P455_R	41	0.88647	0.91554	0.02012	ADCYAP1_P455_R	1.1E+07	NM_001117.2	ADCYAP1	116	18	894932	-455	Y	TCCTGCTGCCCGCTGGTTCCTG[CG]GCTTCTGCTCAGACACCAACGCCA	cg01799816
ADCYAP1_P398_F	42	0.92027	0.90071	0.02568	ADCYAP1_P398_F	1.1E+07	NM_001117.2	ADCYAP1	116	18	894989	-398	Y	TGCCTCTCGGGTGGTACTCCA[CG]CAGGAACCTGAAGAAGCGCTTTG	cg01521573
ALK_P28_F	3111	0.96484	0.95142	0.01971	ALK_P28_F	2.9E+07	NM_004304.3	ALK	238	2	29997964	-28	Y	AGCCGCTGGATCGCATCTGCCTGGG[CG]CCCCCACTTGCAGCTGGCTGAGCCG	cg14528334
ALK_E183_R	31	0.9496	0.93052	0.08589	ALK_E183_R	2.9E+07	NM_004304.3	ALK	238	2	29997753	183	Y	TTCCGAGCACTGGAGCGGCCCGG[CG]GCAGCAGCTGAGGGCGTTCAGG	cg02931220
MATK_P64_F	5744	0.86632	0.94861	0.02574	ALPL_P278_F	1.4E+07	NM_000478.2	ALPL	249	1	21708178	-278	Y	TGCCGACGTTAAAGACAAAACAGGAGACG[CG]CGCAAGGAGCAGGTCAGAGCCAGGC	cg03975786
AR_P54_R	2265	0.93655	0.94172	0.03114	AR_P54_R	5.9E+07	NM_001011645.1	AR	367	X	66680545	-54	Y	AGGAGGCCGGCCCGGTGGGGG[CG]GGACCCGACTCGCAAACTGTGCATTT	cg01329401
ASCL2_P360_F	103	0.93653	0.88374	0.04157	ASCL2_P360_F	4.3E+07	NM_005170.2	ASCL2	430	11	2249118	-360	Y	CCTAGCGCAGCTATGTCCCAG[CG]CGCCCCACCTGTGCGTTAATCTACTGG	cg15376678
ASCL2_E76_R	3019	0.8783	0.91058	0.07886	ASCL2_E76_R	4.3E+07	NM_005170.2	ASCL2	430	11	2248682	76	Y	GGTCTTAGTGCGCCCCAAAGCAAGGTA[CG]CAGGTCCGGGTTGAGCCCTC	cg22073478
ASCL2_P609_R	105	0.89234	0.9354	0.12184	ASCL2_P609_R	4.3E+07	NM_005170.2	ASCL2	430	11	2249367	-609	Y	GGCCTGGAGGTCTGCACCCGAC[CG]CCTTGTCAGGACGGTCAGGT	cg00868120
ATP10A_P147_F	109	0.75108	0.9095	0.04258	ATP10A_P147_F	2.1E+07	NM_024490.2	ATP10A	57194	15	23660110	-147	Y	CCACTTTCAGATTCGTTGTTGGG[CG]AACTAGACCGTTTCTTTCCACC	cg06932470
AXIN1_P995_R	4229	0.88661	0.88109	0.04959	AXIN1_P995_R	3.1E+07	NM_003502.2	AXIN1	8312	16	343460	-995	Y	GGGACCCGACCGCTGCCCG[CG]CGTGAGGGAAGCAGGCTCCCA	cg24498552
FLT1_P615_R	3783	0.85339	0.855	0.10521	B3GALT5_P330_F	1.5E+07	NM_033170.1	B3GALT5	10317	21	39950794	-330	N	GGGGCAGTGACCTAGGCAGAGGG[CG]GGAGCCAGCATGATGGATACACTCAG	cg06700769
APOA1_P261_F	66	0.92691	0.95357	0.22102	B3GALT5_E246_R	1.5E+07	NM_033170.1	B3GALT5	10317	21	39951370	246	N	CACACTCTGGCATCCAG[CG]TCTCCAGCTTGCATGGCCGTGACAGGATT	cg11479877
BCAP31_P1072_F	153	0.95435	0.94779	0.02	BCAP31_P1072_F	4.9E+07	NM_005745.6	BCAP31	10134	X	152644153	.	Y	CCTGACGCGCTCCTGGCTCCTG[CG]GCTGCTGTTCCCGGGTCTGTGCC	cg08372952
BCAP31_P1131_F	152	0.96591	0.96105	0.09832	BCAP31_P1131_F	4.9E+07	NM_005745.6	BCAP31	10134	X	152644212	.	Y	GGGGTGTGGCCCTGCACTCCG[CG]CCTTGGTGAAGCCGCACCTTCTGTCGG	cg05632706
BCR_P346_F	2298	0.9461	0.95875	0.09183	BCR_P346_F	1.1E+07	NM_021574.1	BCR	613	22	21852206	-346	Y	CTCTGACACGACGACTGGGAGTGC[CG]GTGACGCTTATGGCACTGCCG	cg01574123
BCR_P422_F	2304	0.87448	0.91833	0.05543	BCR_P422_F	1.1E+07	NM_021574.1	BCR	613	22	21852130	-422	Y	TGCTCTCCATGGAAGGTGCCCTC[CG]CATCGTTGGGCCAGATCGCTG	cg08146988

JAK3_E64_F	5615	0.95145	0.89473	0.03962	BMP2_P12_01_F	45573_68	NM_0012_00.1	BMP2	650	20	6696006	-1201	Y	AAACTGAAAGTTGAATAACGGGCCAG[CG]GGGAAATAAGAGGCCAGACCCT	cg26536259
BMP2_E48_R	2857	0.91473	0.84151	0.02694	BMP2_E48_R	45573_68	NM_0012_00.1	BMP2	650	20	6697255	48	Y	AATAACTTGCCACCCCACTTTG[CG]CCGGTGCCTTTGCCCAAGCGGAGC	cg18126192
BMP3_P56_R	1700	0.96207	0.96313	0.02144	BMP3_P56_R	45573_70	NM_0012_01.1	BMP3	651	4	82171087	-56	Y	CAGAGCTAGTCTAGTCCCTCG[CG]CGGCCAGTTTGCCGGGTGTTCCCA	cg14573361
BMP3_E147_F	2863	0.89096	0.80967	0.05324	BMP3_E147_F	45573_70	NM_0012_01.1	BMP3	651	4	82171290	147	Y	ACCTGTCAGGCTGCGTGGTTCAG[CG]CAGCAAGTGGGGCTGGCCGCTA	cg06290734
BMP6_P398_F	1888	0.96144	0.96315	0.01645	BMP6_P398_F	48092_81	NM_0017_18.2	BMP6	654	6	7671611	-398	Y	TTCGTGAGCGAGAAGGAAAGTTAAACCT[CG]CGGAATAGACTGGCATTTCCG	cg08280813
BMP6_P163_F	1885	0.95281	0.96481	0.037	BMP6_P163_F	48092_81	NM_0017_18.2	BMP6	654	6	7671846	-163	Y	GCCAGCGAGGCCAGAGTGACCGCGCCG[CG]ACTCGCAGGAGCCAGGGCGCAGG	cg05319903
GABRB3_P92_F	861	0.90471	0.92136	0.19808	CALCA_P75_F	7.7E+0_7	NM_0010_33952.1	CALCA	796	11	14950483	-75	Y	GGCAGTGTCTCTGATGCCTCCAG[CG]CCAGCGACTGCTCTTATTCGCCCG	cg14988155
CCKBR_P361_R	1756	0.9085	0.90338	0.02152	CCKBR_P361_R	3.3E+0_7	NM_1768_75.2	CCKBR	887	11	6237181	-361	Y	GCACGCAGACCTGGTCTCAA[CG]CCACTCCACGTTCCCTGATACA	cg10802353
CCNA1_P216_F	186	0.96601	0.95692	0.07048	CCNA1_P216_F	1.6E+0_7	NM_0039_14.2	CCNA1	8900	13	35904417	-216	Y	CGCCGCTGATTGGCCGATTCAACAGACG[CG]GGTGGGCACTCAGCCGCATCG	cg05780306
CD81_P272_R	220	0.93207	0.94952	0.08141	CD81_P272_R	6.2E+0_7	NM_0043_56.3	CD81	975	11	2354851	-272	Y	ACGCTGCATGCCTGTCTCAGGCG[CG]GCCCTGCTGCCACCCCTTGGG	cg26129028
CDH11_E102_R	172	0.93745	0.943	0.05166	CDH11_E102_R	1.6E+0_7	NM_0017_97.2	CDH11	1009	16	63713318	102	Y	GAGGGTGGACGCAACCTCCGAGC[CG]CCAGTCCCTGGCCAGGGCAAGCG	cg05318914
CDH11_P203_R	3237	0.89733	0.94624	0.06828	CDH11_P203_R	1.6E+0_7	NM_0017_97.2	CDH11	1009	16	63713623	-203	Y	GAGAAGCCGAGGCTGCGAGAGGAG[CG]JAGATGGGCTCGCAGAGGCT	cg23907145
CDH13_E102_F	4061	0.96174	0.96663	0.03082	CDH13_E102_F	6.2E+0_7	NM_0012_57.3	CDH13	1012	16	81218181	102	Y	GTGCATGAATGAAAAACGCCCGGG[CG]CTTCTAGTCGGACAAAATGCAGCCGA	cg15047333
CDH13_P88_F	2356	0.95857	0.97483	0.09479	CDH13_P88_F	6.2E+0_7	NM_0012_57.3	CDH13	1012	16	81217991	-88	Y	CCGTATCTGCCATGCAAAAACGAGGGAG[CG]TTAGGAAGGAATCCGTCTGTAA	cg08977371
CDKN1C_P626_F	240	0.92745	0.93286	0.02301	CDKN1C_P626_F	45574_40	NM_0000_76.1	CDKN1C	1028	11	2864177	-626	Y	CTGCCAGCTCGGCCCTGGCTG[CG]CCGGATGGGGTCTTCGGCTGCCCC	cg17511511
CEACAM1_E57_R	113	0.89529	0.93167	0.01962	CEACAM1_E57_R	6.8E+0_7	NM_0017_12.3	CEACAM1	634	19	47724422	57	N	GAGGAGAGCTTGGGCTCCAGGAA[CG]CTTCGAGCACGGCTGCTCTGTC	cg18176768
CHFR_P635_R	270	0.91787	0.90966	0.02527	CHFR_P635_R	89226_74	NM_0182_23.1	CHFR	5574_3	12	13197489_2	-635	Y	GAAAGAGGAGTAAAGACGGCGAGACG[CG]TCCACGCAGGGGAGTCTGT	cg18592833
CHGA_E52_F	3075	0.95512	0.93044	0.03506	CHGA_E52_F	1.1E+0_7	NM_0012_75.2	CHGA	1113	14	92459297	52	Y	TCGAGCCCCGTGCAGGGGAGCTTG[CG]GGAGGATCGACCGACAGAC	cg15962606
CHGA_P243_F	285	0.84682	0.84175	0.03696	CHGA_P243_F	1.1E+0_7	NM_0012_75.2	CHGA	1113	14	92459002	-243	Y	GGACACAAGGCAATCGGTGGAATCGT[CG]AGGGGTGGAGGATCAGCCACA	cg02706439
COL18A1_P494_R	3245	0.96601	0.96069	0.04085	COL18A1_P494_R	1.9E+0_7	NM_1304_44.1	COL18A1	8078_1	21	45649031	-494	Y	CCCTGCAGGGGCTTGCAGGCG[CG]GAGGTGCCGCTTCCCTCTCCGT	cg00309589
COL18A1_P365_R	3346	0.92406	0.92275	0.01917	COL18A1_P365_R	1.9E+0_7	NM_1304_44.1	COL18A1	8078_1	21	45649160	-365	Y	CGGGCAGCGGTGTTACCTTC[CG]CATAAACCTGGGCTTCTCGCGGGGCA	cg26239725
COL1A1_P5_F	3253	0.96304	0.96757	0.02917	COL1A1_P5_F	1.5E+0_7	NM_0000_88.2	COL1A1	1277	17	45633997	-5	Y	AGAACTCCCTGCTGCTCCGA[CG]ACTGGCCCGGGCCCTTTATACTGTC	cg13069732
COL1A1_P117_R	3366	0.85666	0.91762	0.0676	COL1A1_P117_R	1.5E+0_7	NM_0000_88.2	COL1A1	1277	17	45634109	-117	Y	CGTGCCCGCAATCAGAGCTGCTGGCC[CG]GCCCCAATTGGGAGTTGG	cg10100754
CYP1B1_E83_R	185	0.94313	0.94749	0.06393	CYP1B1_E83_R	1.3E+0_7	NM_0001_04.2	CYP1B1	1545	2	38156713	83	Y	GTTGAGATTGAGACTGGGGT[CG]GTGAGTGGCGTCAAATCCATG	cg09991178

CYP2E1_P416_F	4300	0.81723	0.95481	0.06623	CYP2E1_P416_F	7.6E+07	NM_000773.3	CYP2E1	1571	10	135190441	-416	N	GCTGTTGCCACCAGGAGGGCCGGTAC[CG]TGTCTAGAGGTGGTCGGCATG	cg17336072
DBC1_P351_R	629	0.95722	0.95925	0.07447	DBC1_P351_R	765708	NM_014618.1	DBC1	1620	9	121171873	-351	Y	GCACGAGCATCCAAAGGGACCCGCGCATA[CG]CGCAAACCCGGAATCCTGGTGC	cg14445814
DCC_P471_R	2425	0.92121	0.95308	0.04393	DCC_P471_R	4885174	NM_005215.1	DCC	1630	18	48120685	-471	Y	CCAACAGCATCTCCAGCTCT[CG]CGCGGAATTGTCTCTTCAACTTTACCCA	cg22055405
DIO3_E230_R	3145	0.94028	0.9505	0.15053	DIO3_E230_R	5.6E+07	NM_001362.2	DIO3	1735	14	101097671	230	Y	GGCCTGCAGCCACCATGCTC[CG]CTCCCTGCTGCTTCACTCCTTGAGGCTC	cg18191511
EFNB3_P442_R	1828	0.79569	0.88733	0.01966	EFNB3_P442_R	3.8E+07	NM_001406.3	EFNB3	1949	17	7548803	-442	Y	ACAGGTAGTCGTGACGATCAGCTC[CG]CCGCACTTTGTAAAGCCCAAGCCTTC	cg00000794
EPHA5_E158_R	2693	0.73152	0.93532	0.01927	EPHA5_E158_R	3.3E+07	NM_182472.1	EPHA5	2044	4	66217946	158	Y	GAGAAGGCAGTCCAGAGGGGAGCC[CG]TCGAGGTGCAAGTAGCAGCCGGCC	cg25798792
EPHA8_P256_F	1851	0.8657	0.8678	0.04439	EPHA8_P256_F	5.6E+07	NM_020526.3	EPHA8	2046	1	22762335	-256	Y	GGACGTCCCGATGGTGGCTTCG[CG]CACTGGGGCCCTGAGCCCTG	cg06991945
EPHA8_P456_R	1856	0.89798	0.94211	0.14599	EPHA8_P456_R	5.6E+07	NM_020526.3	EPHA8	2046	1	22762135	-456	Y	TCACCTAAAAGTGCCTCTGAGTTG[CG]CTGAGCCATCTCTGAGCCTTGCCC	cg00665502
EPHB1_E202_R	2903	0.96952	0.95777	0.17325	EPHB1_E202_R	5.6E+07	NM_004441.3	EPHB1	2047	3	135997152	202	Y	GGCTTGTCTCGGCTCGGGC[CG]TCGGCCGGCGATGGCCCTGGATTATCTAC	cg23448029
EPHB6_E342_F	2715	0.91827	0.93442	0.0463	EPHB6_E342_F	5.6E+07	NM_004445.2	EPHB6	2051	7	142263256	342	Y	GGGGCGCAGACCTGCAGAGACTG[CG]GCCAACGGGAAAGGTGAGCC	cg22195019
EPO_E244_R	4087	0.95887	0.93361	0.08985	EPO_E244_R	6.2E+07	NM_000799.2	EPO	2056	7	100156603	244	Y	CGCCCGGTCCCTGTTTGGAG[CG]GGGATTTAGCCTCCGGCTATTGGCC	cg13036038
ERG_E28_F	312	0.96573	0.97438	0.02682	ERG_E28_F	4.6E+07	NM_004449.3	ERG	2078	21	38955460	28	Y	AAAATCCAGCTTACTGTAGCGC[CG]CTCCTCTCTCATGTCCCTCGG	cg12571150
ESR1_E298_R	4092	0.79412	0.93031	0.04717	ESR1_E298_R	6.3E+07	NM_000125.2	ESR1	2099	6	152170677	298	Y	GGCTGTGCTCTTTTCCAGGTGGCC[CG]CCGGTTTCTGAGCCTTCTGCCTGCGG	cg17191385
ER_seq_a1_S60_F	6020	0.90604	0.91376	0.04776	ER_seq_a1_S60_F	6.3E+07	NM_000125.2	ESR1	2099	6	152170860	481	Y	CCCCCTGGAGCGGCCCTGGG[CG]AGGTGTACTGGACAGCAGAAGCCCG	cg16246567
ESR2_E66_F	3262	0.94653	0.95602	0.02824	ESR2_E66_F	1.1E+07	NM_001437.1	ESR2	2100	14	63830765	66	Y	GGCAGTTATTTCTCGCAGCCTC[CG]CGCTTGCAACTGCCTCCTGGCGGGGGA	cg25497024
FABP3_E113_F	3283	0.85851	0.85229	0.03683	FABP3_E113_F	6.3E+07	NM_004102.3	FABP3	2170	1	31618397	113	Y	CTCACCGAGTGACTTCATGTAGTCAT[CG]AAAATCTTGCTGTCCACTAGCTTCCAGGT	cg03365882
ESR2_P162_F	756	0.9495	0.91476	0.02954	FANCE_P356_R	6.7E+07	NM_021922.2	FANCE	2178	6	35527760	-356	Y	CATGACAAGCAACATGCCCTCAG[CG]TAAATACAGCGCGGTCTCTAGCACA	cg04035266
FES_P223_R	4002	0.97334	0.96049	0.25253	FES_P223_R	1.3E+07	NM_002005.2	FES	2242	15	89228490	-223	Y	CGCTGCCGGGCCCTGGGGCCTG[CG]GGGCGGGGCGGCCCTCTTGCTGGGCCATT	cg04362933
FGF3_E198_R	1333	0.96391	0.94374	0.01239	FGF3_E198_R	1.5E+07	NM_005247.2	FGF3	2248	11	69342931	198	Y	CAAAGCGCTGAAAGAAAGGACGGTT[CG]CCAACAAAAGGCCGACGTGGTCC	cg12845334
FGF3_P171_R	5573	0.95042	0.94681	0.02414	FGF3_P171_R	1.5E+07	NM_005247.2	FGF3	2248	11	69343300	-171	Y	GATGACTGATGTCCTGAAAACAACCTG[CG]GGGAAGTCGAGCTGACAAC	cg15119027
FGF6_P139_R	4016	0.93921	0.92309	0.03043	FGF6_P139_R	1E+07	NM_020996.1	FGF6	2251	12	4425180	-139	Y	GAGAGCAGAGGGACCCAGGCTGAGCCG[CG]GCCGGTAGAGACCATGGCTCG	cg01392242
FGF8_P473_F	5683	0.96458	0.8966	0.01376	FGF8_P473_F	1.5E+07	NM_006119.2	FGF8	2253	10	103526290	-473	Y	GCCTGGAGCGCCCGAGTCTGG[CG]GGTCTGGGTCTCCGCTCCGGGCC	cg15208541
FGF8_E183_F	1334	0.79548	0.8894	0.02198	FGF8_E183_F	1.5E+07	NM_006119.2	FGF8	2253	10	103525634	183	Y	CACAGGCAGCTCAGCGCGGAG[CG]GGGGCTGCCATGGCGCGGCCCC	cg02429245
FGFR3_P1152_R	2536	0.85171	0.89158	0.05804	FGFR3_P1152_R	1.3E+07	NM_022965.1	FGFR3	2261	4	1764269	-1152	Y	GCGGGCTCTCAGGCGGCTTAGCTG[CG]TGCGGCCCCAGGTCAGTCAACG	cg12221596

FLI1_P620_R	5708	0.88594	0.91668	0.02488	FLI1_P620_R	71105 92	NM_0020 17.2	FLI1	2313	11	12806857 9	-620	Y	GAGTCTTCCCCGGCAGTAGG[CG]CTGGGTTACCCGCAGC CCTAGCCA	cg26979016
FLT4_P180_R	3804	0.95259	0.94962	0.02357	FLT4_P180_R	45037 52	NM_0020 20.1	FLT4	2324	5	18000935 2	-180	Y	GGCGTCCGGTGCACCCGAGCAGTGC[CG]CTCCGACCA CAGGGTCCGGGCC	cg20020551
TUSC3_P85_R	2164	0.88247	0.79516	0.02074	FN1_E469_F	4.7E+0 7	NM_0540 34.2	FN1	2335	2	21600856 7	469	Y	AACTCAGCCCCAACTTTGGT[CG]GCTTTAGGGTCCCATC CCTGAGGCA	cg01966735
FANCA_P1006_R	3977	0.93506	0.88785	0.18049	FRK_P36_F	3.2E+0 7	NM_0020 31.2	FRK	2444	6	11648865 0	-36	N	CCTGTTTCAAGTCTGTTCTGTCTTT[CG]ACCAGTCCGGAT CTGGACGGCTCTCT	cg18764771
FZD7_E296_F	1600	0.93262	0.95324	0.03523	FZD7_E296_F	45038 32	NM_0035 07.1	FZD7	8324	2	20260785 1	296	Y	TGCTGGGCCACACGAACCAAGAGGAC[CG]GGCCTCGA GGTGCACCAATTCT	cg18631360
FZD9_E458_F	5551	0.96031	0.9613	0.06144	FZD9_E458_F	6.3E+0 7	NM_0035 08.2	FZD9	8326	7	72486503	458	Y	GCGGCTGCCGAGCTAGCGGAGTTCG[CG]CCGCTGGTGCA GTACGGCTGCC	cg25707686
GABRB3_E42_F	3299	0.93339	0.94522	0.12408	GABRB3_E42_F	3E+07	NM_0219 12.2	GABRB3	2562	15	24569978	42	Y	CGGAGCACATGGCGCTGTTCTC[CG]GCCTAACCTGCTG GGATCCGCTCTCC	cg20421990
BRCA1_P835_R	2318	0.79785	0.8718	0.03133	GABRG3_E123_R	1.5E+0 7	NM_0332 23.1	GABRG3	2567	15	25343888	123	N	CCGTACAACCTCCCCTGGGAGA[CG]ACAGCTGGAGGCCCC TGGCTTGTGACTGC	cg16701428
GALR1_E52_F	3314	0.88831	0.92892	0.08589	GALR1_E52_F	60311 65	NM_0014 80.2	GALR1	2587	18	73090773	52	Y	GCTCGGCACCCGTGACTTCTAAGGGG[CG]CGGATTTTCCAG CCGAGCTGTTTTT	cg15343119
GAS7_E148_F	606	0.96563	0.96015	0.02297	GAS7_E148_F	4.1E+0 7	NM_0036 44.2	GAS7	8522	17	10042445	148	Y	CCGGACATGCGCTTGGCGCC[CG]GGTTTACAGCGCAGCC TGCATTCC	cg20649212
GDF10_P95_R	890	0.96436	0.93268	0.06422	GDF10_P95_R	1.2E+0 7	NM_0049 62.2	GDF10	2662	10	48059267	-95	Y	CTCCCCAGCCGAGAGCCCGAGACCCAGCCC[CG]CAGCCG GCTCCTGTGTGTCGG	cg03251024
GML_P281_R	5741	0.94577	0.93603	0.0289	GML_P281_R	45040 32	NM_0020 66.1	GML	2765	8	14391293 8	-281	N	CCTGGCGGTGCCAACAGGCTGC[CG]AGGGTGGCTGCT GTCCCGTTTCTCCAGC	cg20178722
GP1BB_P278_R	926	0.90035	0.94728	0.12377	GP1BB_P278_R	99453 87	NM_0004 07.3	GP1BB	2812	22	18090788	-278	Y	ACACGATGCTCCGTTTTCTTC[CG]TTGTGAATGCCGCGTC CTGCTCTGGTGACA	cg19755554
GSTM2_E153_F	3354	0.96534	0.96129	0.02792	GSTM2_E153_F	2.3E+0 7	NM_0008 48.2	GSTM2	2946	1	11001236 7	153	Y	GGGAAGTGTGGAGCAGCTGCAGGA[CG]GGCTTAGGGA CGGTTCC	cg07246306
GSTM2_P109_R	946	0.90077	0.93174	0.05632	GSTM2_P109_R	2.3E+0 7	NM_0008 48.2	GSTM2	2946	1	11001210 5	-109	N	ATCCTACTCTAGCCCCATGAG[CG]CGCTCCAGGCCTCCA GATTGCC	cg25855733
GUCY2D_E419_R	2999	0.97508	0.9573	0.06611	GUCY2D_E419_R	45042 16	NM_0001 80.1	GUCY2D	3000	17	7847132	419	Y	CGGGTGGGCTTCCGGACCC[CG]GGCTTGGCGTCCCGCG TGGTGGGCTCC	cg13065528
HCK_P46_R	5769	0.94522	0.91455	0.01959	HCK_P46_R	3.1E+0 7	NM_0021 10.2	HCK	3055	20	30103672	-46	Y	GGCGGAGTTAGCTCGCTCAGGG[CG]CGGCTAAGGCGC CCAGATGGCCTGCGG	cg15382497
GFI1_P208_R	4071	0.94598	0.76137	0.0535	HCK_P858_F	3.1E+0 7	NM_0021 10.2	HCK	3055	20	30102860	-858	Y	TGGTGTCTGAATGGAGCAGGCTG[CG]GAAGAGAAACC GCTGACCACAGACC	cg04775393
PDE1B_E141_F	2862	0.91209	0.76279	0.04162	HGF_E102_R	5.9E+0 7	NM_0010 10933.1	HGF	3082	7	81237286	102	N	ATGCCTGGGTGAAAGAATCCTGTT[CG]GAGTCAGTGCCT AAAAGAGCCAGTCC	cg08988647
HHIP_E94_F	2760	0.89836	0.90951	0.0487	HHIP_E94_F	2E+07	NM_0224 75.1	HHIP	6439 9	4	14578671 7	323	Y	GGGGCGCGCTGTGGCAGCACCTCCC[CG]CGCGCTAGTTA AAAAGAAGAAAAG	cg21706827
HHIP_P307_R	2209	0.85502	0.82672	0.04739	HHIP_P307_R	2E+07	NM_0224 75.1	HHIP	6439 9	4	14578631 6	-307	Y	GGCCACTCTTACTTCTTTT[CG]GAGCCTCAGCTTGG CCGCTTTAGCC	cg20605716
NCL_P1102_F	1587	0.96839	0.94693	0.20545	HIC2_P528_R	3.2E+0 7	NM_0150 94.1	HIC2	2311 9	22	20101165	-528	Y	CCCGAGCTTCAGTCACTGCTGGCTG[CG]CCTTTGAGCCT CGGGCAACCGCAG	cg21212889
HLF_E192_F	678	0.93026	0.96722	0.03276	HLF_E192_F	3.2E+0 7	NM_0021 26.3	HLF	3131	17	50697562	192	Y	TGAACATTTTGAAAACGAGGGGTT[CG]AGGCAGGTGAG AGCATCCTGCACGT	cg05876326
HPN_P823_F	4931	0.91936	0.93872	0.21527	HPN_P823_F	3.4E+0 7	NM_1829 83.1	HPN	3249	19	40222427	-823	N	CCTCTGAAAGCAAAGAGAAGTGCACGGG[CG]TCCAGGTG GCCGAATAGCCCTG	cg00566101

HS3ST2_P171_F	1088	0.90519	0.91382	0.03219	HS3ST2_P171_F	51744 62	NM_0060 43.1	HS3ST2	9956	16	22733190	-171	Y	GCCGCCCCGGCTGCCCGGAGCCCCAT[CG]CCTAGGACCGG GAGATGCTG	cg03823653
HS3ST2_E145_R	3482	0.96973	0.96613	0.10827	HS3ST2_E145_R	51744 62	NM_0060 43.1	HS3ST2	9956	16	22733506	145	Y	CGCAGGCTGCTCTTCGCCTTCA[CG]CTCTCGCTCTCTGCA CTTACCTGTGTTAC	cg22228897
ICAM1_P386_R	2658	0.8649	0.9702	0.02083	ICAM1_P386_R	45578 77	NM_0002 01.1	ICAM1	3383	19	10242393	-386	Y	GACTTGAGTTCGGACCCCT[CG]CAGCCTGGAGTCTCAGT TTACCGCTTTGT	cg05106269
ICAM1_E242_F	4104	0.84384	0.85112	0.05366	ICAM1_E242_F	45578 77	NM_0002 01.1	ICAM1	3383	19	10243021	242	Y	GGGAAGGAGGGGCTAGAGACAG[CG]ATTGAAAGGCAAC AGCCAGTAGTTCCG	cg20539223
IGF2_E134_R	4106	0.91127	0.85927	0.02361	IGF2_E134_R	64538 16	NM_0006 12.2	IGF2	3481	11	2116444	134	Y	GGCAGGCGCACAGCGGGAGAGAACAGCA[CG]GAGAGA AACAGAAAGCGTGAATTA	cg10649864
MYOD1_P50_F	1565	0.83851	0.86642	0.09159	IGF2_P103_6_R	64538 16	NM_0006 12.2	IGF2	3481	11	2117614	-709	Y	CCACCAGGAGGCTGCACTGCGGGT[CG]CCCCGTCTGAG TGCAGATGCAGT	cg04741015
IGF2AS_P203_F	1110	0.85876	0.94487	0.15062	IGF2AS_P203_F	77059 72	NM_0164 12.1	IGF2AS	5121 4	11	2118120	-203	Y	GGAAACCATCTCTGGAGAGTTTAA[CG]ATGTAAGAAA GCACTGTGATTTTACC	cg14188639
PLXDC2_P914_R	2776	0.77683	0.75237	0.03634	IGFBP1_P12_R	6.2E+0 7	NM_0010 13029.1	IGFBP1	3484	7	45894472	-12	Y	CCTCCCACCGGTTT[CG]TAGGGCTTGGGTGCACT AGCAAAACAAAC	cg00110785
IGFBP1_E48_R	4111	0.96022	0.96911	0.26009	IGFBP1_E48_R	6.2E+0 7	NM_0010 13029.1	IGFBP1	3484	7	45894532	48	Y	ATTTTGAACACTCAGCTCCTAGCGT[CG]GCGCTGCCAAT CATTAACTCCTGGTGC	cg20666158
IGFBP2_P306_F	5664	0.91871	0.85053	0.03587	IGFBP2_P306_F	5.6E+0 7	NM_0005 97.2	IGFBP2	3485	2	21720606 6	-306	Y	AGGGGAAGCGCGAAACGAACTG[CG]CGAACTGAAC TGAGAGCAGACAAAAG	cg20018535
IGFBP7_P371_F	1111	0.90505	0.96992	0.02727	IGFBP7_P371_F	45046 18	NM_0015 53.1	IGFBP7	3490	4	57671667	-371	Y	AAACTTCTTAACAACCAACCGCTT[CG]AGACGATCCAGGGT TTCATCTATTAATC	cg16546204
SNURF_P2_R	2037	0.88547	0.83294	0.02871	IGSF4_P45_4_F	2.2E+0 7	NM_0143 33.2	IGSF4	2370 5	11	11488077 9	-454	Y	GCACACCGAGTGCATCTGGCCTAG[CG]AACCCAGACGTTG CAAATTTCCGTCA	cg05357252
IHH_E186_F	5583	0.9627	0.95505	0.02377	IHH_E186_F	5.1E+0 7	NM_0021 81.1	IHH	3549	2	21963324 7	186	Y	TCTTGCTTCATAGCGTCCGCTGG[CG]CCAGGGTCTTCT CGGGCACATTGGG	cg27171516
IL11_P11_R	4188	0.91231	0.90851	0.05576	IL11_P11_R	2.4E+0 7	NM_0006 41.2	IL11	3589	19	60573637	-11	Y	GAGGCATGTGCCCTGAGCAGCAGGGCCG[CG]GCAGTGA GGGAGTGTGGAC	cg16546221
ITPR2_P804_F	1248	0.89395	0.89754	0.12339	IL16_P226_F	2.7E+0 7	NM_0045 13.3	IL16	3603	15	79262029	-226	N	TCAAGGAGGGCAGGAGTTGGAAG[CG]ACCGTTGTAAA CGTTAAAGATTT	cg12993983
FLI1_E29_F	1337	0.96972	0.95441	0.09212	IL6_P213_R	1.1E+0 7	NM_0006 00.1	IL6	3569	7	22733132	-213	N	TCTGCTTCTTAGCGCTAGCCTCAATGA[CG]ACCTAAGCTG CACTTTTCCCCTAG	cg13802710
IL6_E168_F	4118	0.94221	0.92793	0.09103	IL6_E168_F	1.1E+0 7	NM_0006 00.1	IL6	3569	7	22733513	168	N	GTGTGGCCAGGGAGGGCTGG[CG]GGCGGCCAGCAGCA GAGGCAGGC	cg05401786
INHA_P1144_R	5800	0.964	0.96469	0.02158	INHA_P1144_R	92572 23	NM_0021 91.2	INHA	3623	2	22014405 4	.	Y	CGAGGCCCCAGCTGTGCC[CG]CCCTTCTCCACACCAC TACA	cg01858402
INHA_P1189_F	5715	0.96511	0.9387	0.0218	INHA_P1189_F	92572 23	NM_0021 91.2	INHA	3623	2	22014400 9	.	Y	GGTCAGCAGCAGGCCGTGCTCCGCGC[CG]TCCCGCGGA AGCTCAGGC	cg16613202
CSF3R_P8_F	3463	0.94755	0.96665	0.24032	INS_P248_F	45576 70	NM_0002 07.1	INS	3630	11	2139248	-248	N	CATTAGAGCTTAACCCAGGGCC[CG]GTGGCCAGACCTG TCCCTGCTACA	cg24338752
KCNK4_E3_F	3534	0.94351	0.94582	0.16036	KCNK4_E3_F	1.6E+0 7	NM_0166 11.2	KCNK4	5080 1	11	63815454	3	Y	GAGATGCCAGATTAGCGTGGTGCCTG[CG]GAGAGACG GGCCAGCTGATG	cg01352108
KDR_E79_F	800	0.88824	0.95652	0.01904	KDR_E79_F	1.1E+0 7	NM_0022 53.1	KDR	3791	4	55686440	79	Y	AGGCTGCCAGACGGACTTTCTGCGG[CG]CGCAAGTGTG CCCGCCGAGGCAGA	cg10740902
KDR_P445_R	4232	0.92829	0.95367	0.17622	KDR_P445_R	1.1E+0 7	NM_0022 53.1	KDR	3791	4	55686964	-445	Y	TGCAGCAGTTGGAGCCACAAGGGAGAAG[CG]GATACTC AGCCAAGTATGCCGGTC	cg04695981
KIT_P405_F	4020	0.95513	0.96721	0.0359	KIT_P405_F	45576 94	NM_0002 22.1	KIT	3815	4	55218513	-405	Y	GAGCACCTGGCAGGTGGCGGGCC[CG]TGCCCTAACGTGT GCGTGGTG	cg27154163

KIT_P367_R	4019	0.93968	0.96288	0.04486	KIT_P367_R	45576 94	NM_0002 22.1	KIT	3815	4	55218551	-367	Y	CGGTGGTGCCAGCTTCACAAAG[CG]AGCGGGCAGCACC TCCTTGTGTCGG	cg23927351
L1CAM_P19_F	5719	0.94991	0.95238	0.04188	L1CAM_P1 9_F	1.3E+0 7	NM_0240 03.1	L1CAM	3897	X	15279452 4	-19	Y	CAGCACAGCCAGCCGGGCT[CG]GTTCAAGGCTCCGGCCGG AGGGG	cg12024667
LAT_E46_F	3562	0.8336	0.86268	0.04238	LAT_E46_F	6.3E+0 7	NM_0143 87.3	LAT	2704 0	16	28903694	46	N	GGGTCTGGATATGGAGGCCA[CG]GCTGCCAGCTGGCA GGTGGC	cg03108875
LOX_P71_F	1309	0.95909	0.95786	0.14437	LOX_P71_F	2.1E+0 7	NM_0023 17.3	LOX	4015	5	12144192 4	-71	Y	AGTTACACAAGCCGTTCTGGCC[CG]GCCGCCCTCAGCTA TTTGTTCAC	cg03619973
LRP2_E20_F	3574	0.94737	0.93714	0.02499	LRP2_E20_F	68069 18	NM_0045 25.1	LRP2	4036	2	16992723 9	20	Y	GCACCGGCAGCGCCTCTGCTAG[CG]AACGCTCCTTAGGT CTGCACCTCCG	cg10022744
LY6G6E_P45_R	1321	0.87018	0.95067	0.16775	LY6G6E_P4 5_R	1.3E+0 7	NM_0241 23.1	LY6G6E	7913 6	6	31789613	-1499	N	AATCTGGGAGAGGTGATCTGCACC[CG]AGATCCGGGA TTTGTAGAGTT	cg26399860
MAF_P826_R	4251	0.9752	0.95993	0.08062	MAF_P826_R	7.3E+0 7	NM_0053 60.3	MAF	4094	16	78192938	-826	Y	GTGCCCTTGACAGAGCGAGCCCTATG[CG]AGATAACT CCGGGGAAGCTCAA	cg24274831
MATK_P190_R	5839	0.93549	0.8797	0.08751	MATK_P19 0_R	2.1E+0 7	NM_1393 55.1	MATK	4145	19	3753000	-190	Y	CTCCCGGGCATAAGGAAGGAAG[CG]GGGCTGCAGGTA CCGCCTG	cg21380287
MMP2_P303_R	4151	0.9401	0.94071	0.02568	MMP2_P30 3_R	7.6E+0 7	NM_0045 30.2	MMP2	4313	16	54070286	-303	Y	CCGGCGTCCCTCTAGTAGTAC[CG]CTGCTCTAACCTC AGGACGTCAAGG	cg20640526
MMP2_E21_R	925	0.94352	0.95435	0.05386	MMP2_E21_R	7.6E+0 7	NM_0045 30.2	MMP2	4313	16	54070610	21	Y	CGGCTGCCCTCCCTTGTTC[CG]CTGCATCCAGACTTCTC AGGCGGT	cg16119420
MMP2_P197_F	4307	0.91731	0.90587	0.02511	MMP2_P19 7_F	7.6E+0 7	NM_0045 30.2	MMP2	4313	16	54070392	-197	Y	GCGAGAGAGGCAAGTGGGGTGA[CG]AGGTCGTGCACTG AGGGTG	cg20597545
MSH2_P1008_F	2768	0.92087	0.9039	0.04807	MSH2_P10 08_F	45577 60	NM_0002 51.1	MSH2	4436	2	47482759	-1008	Y	ACTGGGATTATGGCGTGTGACACCA[CG]CCTGGCGTCAA ACGTTTGTCTT	cg20331910
MT1A_P49_R	1564	0.96753	0.95118	0.01084	MT1A_P49_R	7.1E+0 7	NM_0059 46.2	MT1A	4489	16	55230030	-49	Y	GCAGGGCGGGTCTTTGCGTC[CG]GCCCTTTCCCTGA CCATAA	cg22243129
MT1A_E13_R	3695	0.86559	0.92754	0.05199	MT1A_E13_R	7.1E+0 7	NM_0059 46.2	MT1A	4489	16	55230092	13	Y	GCCCTACCAAGCCTTCCA[CG]TGCGCTTATAGCCTCTCA ACTTCTTGCTT	cg26001009
MT1A_P600_F	1563	0.94515	0.95914	0.16103	MT1A_P60 0_F	7.1E+0 7	NM_0059 46.2	MT1A	4489	16	55229479	-600	Y	AGAGTGAGAGGCGACCCGTGTTC[CG]TGTTACTGTGT ACGGAGTAGTGG	cg10731123
MYCN_E77_R	4150	0.93173	0.84629	0.01851	MYCN_E77_R	6.3E+0 7	NM_0053 78.4	MYCN	4613	2	15998211	77	Y	GCCGAGCAAGCGCTAGCCAGG[CG]CAAGCGCACAGA CTGTAGCATCC	cg02204046
MYH11_P22_F	2152	0.97163	0.97665	0.02199	MYH11_P2 2_F	1.3E+0 7	NM_0228 44.1	MYH11	4629	16	15858391	-22	Y	GGAGCGTCCAAATCTCCCTG[CG]CGTCTCGGACGCTCT CTTATAGAC	cg15581089
MYH11_P236_R	2403	0.95965	0.91829	0.02509	MYH11_P2 36_R	1.3E+0 7	NM_0228 44.1	MYH11	4629	16	15858605	-236	Y	GCACCGCACAAGGGCGCACGGAACAGGTG[CG]CACAGG GACGGGAGTCTCAGCCC	cg21571155
NEFL_P209_R	1596	0.95645	0.92109	0.02391	NEFL_P209_R	54537 61	NM_0061 58.1	NEFL	4747	8	24870155	-209	Y	GGGGCAGCGCGTCTGCAGCCAAGG[CG]AGGATTCTG CGCAAAAGGGA	cg05876319
NEFL_E23_R	3711	0.94225	0.92657	0.09619	NEFL_E23_R	54537 61	NM_0061 58.1	NEFL	4747	8	24869923	23	Y	CGCCGCTGTAGGAGGTGAGTAGTA[CG]GCTGTAGCT GAAGAACTCATG	cg00987688
HIC- 1_seq_48_S103 _R	6059	0.94617	0.95574	0.16664	NES_P239_R	3.8E+0 7	NM_0066 17.1	NES	1076 3	1	15491405 2	-239	N	GAGGCTGTGAAGAAGGGTCAATCC[CG]AAAAAGGC AGATAATGCACAGAACTGA	cg17059112
NGFB_E353_F	3030	0.96376	0.97219	0.01931	NGFB_E353_F	7.1E+0 7	NM_0025 06.2	NGFB	4803	1	11568202 7	353	Y	CGCGTTATCCACTTCTAGCCCT[CG]AGTAGACCTGGCA TGGCCGTGGGCTTCT	cg02459758
NGFB_P13_F	2157	0.95643	0.96631	0.19021	NGFB_P13_F	7.1E+0 7	NM_0025 06.2	NGFB	4803	1	11568239 3	-13	Y	CCAGCGTCTCTGCTGTGCGGAG[CG]CCGAGCTGCTCTC ACACAGGCTTCTGAA	cg11660906



NPR2_P618_F	2439	0.90643	0.78266	0.02158	NPR2_P618_F	7.4E+07	NM_0039_95.3	NPR2	4882	9	35781788	-618	Y	CGCCGTAGCTCCGGATGGGACCAG[CG]CCCAGGCCCCGTTAGTCCAAGCAGG	cg02519855	
NTRK3_E131_F	991	0.95185	0.96127	0.03736	NTRK3_E131_F	6E+07	NM_0025_30.2	NTRK3	4916	15	86600534	131	Y	CCTCTGCCTTTGAAACGCCGAG[CG]ATCAGATGCAAAATCCTTCAGCGTCTG	cg00865584	
NTRK3_P752_F	4957	0.89453	0.92387	0.03437	NTRK3_P752_F	6E+07	NM_0025_30.2	NTRK3	4916	15	86601417	-752	Y	CCTTCCACTTTTTGGCCCT[CG]CGCTACCCGGTTTTGCTGCAATCCGGA	cg09147530	
NTRK3_P636_R	4224	0.93452	0.90313	0.02844	NTRK3_P636_R	6E+07	NM_0025_30.2	NTRK3	4916	15	86601301	-636	Y	CGCTAGCCGAGCCCGGGGAAAC[CG]AGACCGAAGGGAAAAAGTTGCA	cg25116345	
OGG1_E400_F	936	0.92978	0.96373	0.09427	OGG1_E400_F	8670539	NM_0168_28.1	OGG1	4968	3	9766105	400	Y	GATGGAGTATGGAAGAATGCCAAGA[CG]GCAGGCAGCAGCTGTGCCGGCC	cg10816847	
OPCML_E219_R	3737	0.93948	0.95663	0.03191	OPCML_E219_R	6E+07	NM_0025_45.3	OPCML	4978	11	13290739	4	219	Y	TGGGATGAAGAGCAGGGCAGTTGT[CG]CCGAGAAGACGACCCAGTAGGCAGG	cg19151121
P2RX7_P597_F	2173	0.89004	0.96614	0.15883	P2RX7_P597_F	3.4E+07	NM_1774_27.2	P2RX7	5027	12	12005446	4	-597	N	TTGGCTGATTGGTCTAGGTATAGAT[CG]ACCTGCCGGGGTGCAGAGG	cg08688169
PALM2-AKAP2_P420_R	5114	0.95722	0.93943	0.02282	PALM2-AKAP2_P420_R	2.2E+07	NM_1471_50.1	PALM2-AKAP2	445815	9	111581990	-550	Y	GGGTCCACATTCGGTCAGA[CG]CCCCTCCTACTGGCATCTGCC	cg12992456	
PALM2-AKAP2_P183_R	5117	0.9177	0.88537	0.06245	PALM2-AKAP2_P183_R	2.2E+07	NM_1471_50.1	PALM2-AKAP2	445815	9	111582227	-313	Y	GGTCCATCACACTCCAGGGG[CG]GAGCGAGGCACCGAGACGTCAGGGC	cg21898539	
PAX6_P50_R	1665	0.93757	0.94407	0.02166	PAX6_P50_R	7.1E+07	NM_0016_04.3	PAX6	5080	11	31789505	-50	Y	GCTTTATGCAAAGCAGCGCCGGGGCCT[CG]CGCCAGCCGATTGGATGCTCCC	cg06727689	
PDE1B_P263_R	2612	0.96781	0.96626	0.03136	PDE1B_P263_R	2.4E+07	NM_0009_24.2	PDE1B	5153	12	53229408	-263	Y	CGCCTCCGCTGCACTCTGTAACA[CG]CACTCACATCCGCAGTACAGGGC	cg06901488	
PDGFRA_P1429_F	4234	0.85915	0.88732	0.02896	PDGFRA_P1429_F	6.2E+07	NM_0062_06.3	PDGFRA	5156	4	54788775	-1429	Y	GCTGAAGATGCACGAGAGCGGTTCTG[CG]TAGAAGAAGTCCGCAATGGC	cg27645880	
PDGFRB_P343_F	2808	0.88897	0.87776	0.01664	PDGFRB_P343_F	6.8E+07	NM_0026_09.3	PDGFRB	5159	5	149515958	-343	Y	CACTTTCCGATGCCATGT[CG]GGTGGCGCCCTCCCTTGCATGGC	cg25440811	
PDGFRB_E195_R	4153	0.92604	0.90477	0.04758	PDGFRB_E195_R	6.8E+07	NM_0026_09.3	PDGFRB	5159	5	149515420	195	N	AAGCATCCTTCGGGAGGAGCAGAGC[CG]CCAGAGGGGC	cg21817429	
PDGFRB_P273_F	2810	0.82161	0.89512	0.10057	PDGFRB_P273_F	6.8E+07	NM_0026_09.3	PDGFRB	5159	5	149515888	-273	Y	CTTAGAAATTCACAGCCA[CG]CCAGCCGCCAGCTGCTGAGTCACTTTT	cg12727795	
PENK_E26_F	3752	0.95902	0.95171	0.0422	PENK_E26_F	4E+07	NM_0062_11.2	PENK	5179	8	57521117	26	Y	TTGAGCCTGCCTGGGCGAGAA[CG]GGGTCCCTCGGCAAGACCTC	cg25021837	
PENK_P447_R	1678	0.84465	0.88918	0.0376	PENK_P447_R	4E+07	NM_0062_11.2	PENK	5179	8	57521590	-447	Y	CAAATTGAAAAGCCGGTTTCAGACA[CG]ACTCTAGAGGGAAGAGAAGAAG	cg07433146	
PI3_E107_F	3778	0.80627	0.91406	0.07173	PI3_E107_F	3.2E+07	NM_0026_38.2	PI3	5266	20	43237019	107	N	CTTGATCGTGGTGGTTCCTCAT[CG]CTGGGACGCTGGTTCTAGAG	cg17976697	
PLXDC1_E71_F	2871	0.8306	0.85677	0.02792	PLXDC1_E71_F	2.1E+07	NM_0204_05.3	PLXDC1	57125	17	34561227	71	Y	AGCTCGCCTCGCATGGTGGGTGCC[CG]GACCTGCCCCCGGCTGCTGCTG	cg26456838	
PLXDC1_P236_F	2732	0.91293	0.96019	0.13789	PLXDC1_P236_F	2.1E+07	NM_0204_05.3	PLXDC1	57125	17	34561534	-236	Y	CGCCTGCCCTCAGCCCTAA[CG]GAGCGCTCCCTAGAGCTCTGACCC	cg21125376	
PLXDC2_E337_F	3051	0.97407	0.9719	0.03212	PLXDC2_E337_F	4E+07	NM_0328_12.7	PLXDC2	84898	10	20145715	337	Y	GCTGCCGAGTGAACCGACAGTTTG[CG]AGCCTCGGCTGCAAGTGGCCTC	cg16953926	
POMC_P53_F	1741	0.95149	0.962	0.01463	POMC_P53_F	4505948	NM_0009_39.1	POMC	5443	2	25245009	-53	Y	ACTTCCGAGCTCTCTGGTGGGCG[CG]GGACTTTGACCTTCCCGGAGCAC	cg00293936	
POMC_P400_R	1743	0.95313	0.96328	0.09494	POMC_P400_R	4505948	NM_0009_39.1	POMC	5443	2	25245356	-400	Y	TGGTTCGATTTGGCGGTAATATCAC[CG]TCTGCACAGGGAGGCCTCC	cg22632966	

PROK2_P390_F	1765	0.95823	0.95534	0.01635	PROK2_P390_F	2.4E+07	NM_021935.2	PROK2	60675	3	71917292	-390	Y	CCGGAACCGCTTTTGTGGTCTC[CG]AGACACTCATTGTCTCCTGGTTTCCAA	cg01645467	
PROK2_E0_F	3826	0.87788	0.91728	0.01957	PROK2_E0_F	2.4E+07	NM_021935.2	PROK2	60675	3	71916902	0	Y	CAGGCTCCTCATGGCCCT[CG]GGACTGGGCGGCCCGCCGGAGGCAG	cg12848837	
PTCH2_P37_F	5025	0.97279	0.96675	0.05367	PTCH2_P37_F	5.2E+07	NM_003738.3	PTCH2	8643	1	45081240	-37	Y	CCCAACCCGCGTTATCTGGG[CG]CTCCATAGGCTAGCCC	cg02059556	
PTPRH_P255_F	5067	0.94259	0.91241	0.12495	PTPRH_P255_F	6.7E+07	NM_002842.2	PTPRH	5794	19	60412909	-255	N	TGACCCAGGTACCGGTGC[CG]CGCCCACTGCTGCA	cg17314748	
PURA_P928_R	5960	0.94219	0.8783	0.0283	PURA_P928_R	6.3E+07	NM_005859.3	PURA	5813	5	139472964	-928	Y	GCCCTGGTGCCTACTGCTCTGCT[CG]GCTCCCCCA	cg13473072	
RARB_E114_F	4165	0.96889	0.97305	0.05175	RARB_E114_F	1.5E+07	NM_016152.2	RARB	5915	3	25444872	114	Y	GAGGACTGGGATGCCGAGAACG[CG]AGCGATCCGAGCA	cg14265392	
ASCL1_E24_F	3014	0.95371	0.93388	0.0199	RARB_P60_F	1.5E+07	NM_016152.2	RARB	5915	3	25444698	-60	Y	CTAGTTGGGTCATTGAAGTTAGCAGCC[CG]GGTAGGG	cg06720425	
RASGRF1_E16_F	3860	0.96776	0.96739	0.01408	RASGRF1_E16_F	2.5E+07	NM_002891.3	RASGRF1	5923	15	77169879	16	Y	GCGACGTGGCCATCATTGAGC[CG]GATCCCTCTGTCATG	cg16752670	
RET_seq_53_S374_F	6099	0.78711	0.77199	0.0153	RET_seq_53_S374_F	5.1E+07	NM_020630.3	RET	5979	10	42892087	-446	Y	GCGGGTGCACCCGAGCAGT[CG]GCCAGACCTGCAT	cg01812049	
SCGB3A1_E55_R	3888	0.97154	0.95776	0.03947	SCGB3A1_E55_R	5E+07	NM_052863.2	SCGB3A1	92304	5	179951038	55	Y	CTACCGGAGCTGACGAGACGGGCCA[CG]CAGAGCCCCA	cg19421379	
SCGB3A1_P103_R	1883	0.89138	0.90797	0.0991	SCGB3A1_P103_R	5E+07	NM_052863.2	SCGB3A1	92304	5	179951196	-103	Y	GCGTCTGAGAAAGCCCTGCCGCT[CG]CTCACGGCC	cg11379125	
SEPT5_P441_F	5988	0.80378	0.85643	0.02082	SEPT5_P441_F	5.8E+07	NM_00109939.1	SEPT5	5413	22	18081546	-441	Y	GTCTGCTCGCAGCAGGTCTGCGCAGCAC[CG]AGCGGT	cg11788728	
SEPT9_P58_R	6002	0.9611	0.96435	0.02458	SEPT9_P58_R	2E+07	NM_006640.2	SEPT9	10801	17	72827686	-58	Y	CCGGTGGTCTGCCGACTCCT[CG]GGGCCACTTCGGGC	cg05428394	
GJB2_P791_R	897	0.9011	0.84682	0.08744	SERPINA5_E69_F	3.4E+07	NM_000624.3	SERPINA5	5104	14	94117633	69	N	CCCAGGCTTGAGGGCATGTGAGG[CG]AGGAGAGGATG	cg08764227	
SEZ6L_P299_F	1931	0.91061	0.93923	0.01792	SEZ6L_P299_F	5.6E+07	NM_021115.3	SEZ6L	23544	22	24895181	-299	Y	TGGCCAGGCAGAGCTGCTGGGAG[CG]TCAGCAGGAGAGA	cg09131631	
SEZ6L_P249_F	1935	0.94926	0.90339	0.02042	SEZ6L_P249_F	5.6E+07	NM_021115.3	SEZ6L	23544	22	24895231	-249	Y	GCTCCAGGACGCAAGGGGAATTGG[CG]TTAACTTTGC	cg20207331	
SFRP1_E398_R	3910	0.96365	0.95574	0.01458	SFRP1_E398_R	5.6E+07	NM_003012.3	SFRP1	6422	8	41285739	398	Y	TGTCGACTGGAAGCTCACGTAGTCTGACT[CG]CTGGCC	cg27086426	
SFRP1_P157_F	1946	0.93621	0.94547	0.01521	SFRP1_P157_F	5.6E+07	NM_003012.3	SFRP1	6422	8	41286294	-157	Y	GCGGTTTCGTTTACTAGAACCAGA[CG]CGGCTCAACAC	cg15881237	
SFTPA1_E340_R	3913	0.83449	0.96792	0.05811	SFTPA1_E340_R	3.9E+07	NM_005411.3	SFTPA1	6435	10	81361004	340	N	GGGGCCAGGCTGCGGGCC[CG]TTCATCTTTTTTCTTCT	cg17981088	
SGCE_P250_R	1969	0.9236	0.93371	0.02864	SGCE_P250_R	1.1E+07	NM_003919.1	SGCE	8910	7	94123664	40	Y	GGTGTGTGTCGAAGAACTGACTG[CG]CCCTGAGGAGA	cg26050163	
CYP2E1_E53_R	5510	0.89768	0.86957	0.11266	SHH_E328_F	2.1E+07	NM_000193.2	SHH	6469	7	15529740	0	328	Y	GATCTTCCCTTACACTT[CG]CTGGCCTAGGGTCTTC	cg02023134
IHH_P246_R	4944	0.89263	0.79082	0.0474	SHH_P104_R	2.1E+07	NM_000193.2	SHH	6469	7	155297832	-104	Y	ATGGCAGGCTGCCGGCGCTGATAA[CG]GAACACATCGG	cg06981396	
SLC22A3_E122_R	3926	0.95052	0.95329	0.02129	SLC22A3_E122_R	2.4E+07	NM_021977.2	SLC22A3	6581	6	160689537	122	Y	CTGCTGTGCTGACGGGCTCACCTT[CG]CCTTCTCTTC	cg01037838	
SLC6A8_P193_R	2016	0.81747	0.80866	0.06519	SLC6A8_P193_R	5032096	NM_005629.1	SLC6A8	6535	X	152606393	-193	Y	GTAGCAACCTCTGCTCC[CG]CTGGAGCGGCTCTCCT	cg19792609	

FLT1_E444_F	515	0.89118	0.91121	0.17518	SMAD2_P8_48_R	5.1E+07	NM_0059_01.3	SMAD2	4087	18	43712069	-848	Y	GGGTCTTGGAGAGCACTTAGGGCC[CG]GGTAGGGGATGCCAGGTATAA	cg02100834
SNRPN_seq_18_S99_F	6124	0.93254	0.95828	0.02789	SNRPN_seq_18_S99_F	3E+07	NM_0228_06.2	SNRPN	6638	15	22751285	57	Y	CGCATCTGTCTGAGGAGCGGTCACTGTA[CG]CGATGGAGCGGGCAAGGTCACTGTGCCGG	cg10146073
SNRPN_seq_12_S127_F	6123	0.95967	0.93338	0.04561	SNRPN_seq_12_S127_F	3E+07	NM_0228_06.2	SNRPN	6638	15	22751217	-11	Y	GTGTGCGAAGCCTGCCGTGTCTGAG[CG]AGTCTGGCGCAGAGTGGAGCG	cg05182424
SNURF_E256_R	3937	0.94436	0.94727	0.03019	SNURF_E256_R	3E+07	NM_0056_78.3	SNURF	8926	15	22751484	256	Y	AGGCTTGTCTGTTGTCGGTTCTGCC[CG]ATGGTATCTGTCCGCTCGATTGGGGCG	cg07995992
SNURF_P78_F	2035	0.9684	0.96586	0.10681	SNURF_P78_F	3E+07	NM_0056_78.3	SNURF	8926	15	22751150	-78	Y	CCTGCACTGCGGCAAAACAGCACGCTGCG[CG]GCCGCAAGAGGAGCTGGCC	cg15999943
CCND2_P887_F	2329	0.88177	0.87764	0.10202	SOD3_P460_R	4507150	NM_0031_02.1	SOD3	6649	4	24404693	-460	N	TAGCACAAAGTCTAGAATACCAGAA[CG]GAGACGTGCTTCTTGACCTTAAACGAAA	cg16986592
SOX1_P294_F	5935	0.82265	0.92925	0.08852	SOX1_P294_F	3E+07	NM_0059_86.2	SOX1	6656	13	11176962	-294	Y	GGGCCGGGCCAGCGCACCCGCTCC[CG]GCCCAAAAGCGGAGCTGCAACT	cg23071766
SOX1_P1018_R	5941	0.86896	0.88147	0.12704	SOX1_P1018_R	3E+07	NM_0059_86.2	SOX1	6656	13	11176889	-1018	Y	CACGACGATCCTTTCTTAGTCTT[CG]CTTTTCAACCAATCGTTAATCATT	cg14311093
SOX17_P287_R	5958	0.92088	0.96132	0.04578	SOX17_P287_R	3.1E+07	NM_0224_54.2	SOX17	6432	8	55532761	-287	Y	TTCATCTAAACGACCTTGGGCAAGTA[CG]TCGATTCCAAGGTACAATCAGCC	cg19346665
SOX17_P303_F	5943	0.88557	0.92136	0.07668	SOX17_P303_F	3.1E+07	NM_0224_54.2	SOX17	6432	8	55532745	-303	Y	GAATGGACGCTCGGTATGTTTCATCTAAA[CG]ACCTGGGCAAGTACGTCGATT	cg09626193
SPARC_P195_F	5009	0.88781	0.92023	0.16724	SPARC_P195_F	4.9E+07	NM_0031_18.2	SPARC	6678	5	15104690	-195	N	ACCCTGCCTGCCTCATCTGTT[CG]GGGCTGCTGCCTAAACCGACTCACAGAG	cg01524697
PARP1_P610_R	5915	0.83663	0.83248	0.03113	ST6GAL1_P528_F	2.8E+07	NM_1732_16.1	ST6GAL1	6480	3	18813068	-528	Y	GCCGGTAGCAGAGACCGGGTGTACAGCAC[CG]CATGTTAGGACAAAAGCCGGACACTG	cg27158598
STK23_E182_R	3962	0.95656	0.95889	0.07526	STK23_E182_R	6.3E+07	NM_0143_70.2	STK23	2657	6	15269988	182	Y	CACAGCCTCCTGCGGGCC[CG]AGTCTCGGGCTCCGAACTAGCCC	cg02910024
STK23_P24_F	2059	0.93619	0.89725	0.04122	STK23_P24_F	6.3E+07	NM_0143_70.2	STK23	2657	6	15269968	-24	Y	GCCAAGGCTATAAATTCGCAGGCCGCGG[CG]GGCCCCACAGGACGCGCCCG	cg15753733
TAL1_P594_F	5221	0.87274	0.96185	0.0539	TAL1_P594_F	4507362	NM_0031_89.1	TAL1	6886	1	47468624	-594	Y	TCACACATCGAAGTCTTGATTAAC[CG]AAGGCTCCTTCTATTTGCCGCGCTT	cg13537642
TAL1_E122_F	1055	0.85792	0.82896	0.09433	TAL1_E122_F	4507362	NM_0031_89.1	TAL1	6886	1	47467908	122	Y	CCGACAGGCTGTCTGGAACATTTT[CG]AACCTCCAACCTGGATCGGTCTGGTT	cg00875272
TBX1_P885_R	5961	0.95466	0.96698	0.07874	TBX1_P885_R	1.8E+07	NM_0806_46.1	TBX1	6899	22	18123341	-885	Y	CTCAGTCTCCCTTTGCACGGT[CG]CGGCGGAGCCCGATTCTGCTCTCTCC	cg03402455
TCF4_P175_R	5246	0.9061	0.88891	0.04648	TCF4_P175_R	4507398	NM_0031_99.1	TCF4	6925	18	51406615	-175	Y	TCGGGCAGGCTAGGATGATCCCCCT[CG]CACCCACCCCGAGGGGAAAAA	cg19706341
TERT_P360_R	2885	0.95768	0.96113	0.04814	TERT_P360_R	3.8E+07	NM_1982_55.1	TERT	7015	5	1348519	-360	Y	CGAGGGCCCCAGCGGAGAGAGGT[CG]AATCGGCCTAGGCTGTGGG	cg17903235
TGFBI_P31_R	5310	0.88314	0.83699	0.02027	TGFBI_P31_R	4507466	NM_0003_58.1	TGFBI	7045	5	13539256	-31	Y	GCTTACTTAACCTGCCCCGGGCGG[CG]GAGCGCTCTCATCTCCCTGGAGCC	cg07852148
THPO_P585_R	5322	0.93472	0.92072	0.21166	THPO_P585_R	4.1E+07	NM_1992_28.1	THPO	7066	3	18557921	-585	N	TGTCAGGTGCGGGGCACATGTATGTG[CG]CACACGTGCACTGGGTTAAGCCTGAG	cg20482454
THY1_P149_R	5973	0.88663	0.90083	0.11095	THY1_P149_R	2E+07	NM_0062_88.2	THY1	7070	11	11879923	-149	Y	GGAAGGAAGAGAAGCGGTC[CG]CATTGGTGTGAGAGTGGCAGG	cg18809507
TIMP3_seq_7_S38_F	6126	0.96726	0.96024	0.05882	TIMP3_seq_7_S38_F	7.6E+07	NM_0003_62.4	TIMP3	7078	22	31527437	.	Y	GAGGGCTCCGCTCCGAGGACCCAG[CG]GCAAGCACCCGGTCCCGGC	cg04421373

TNFRSF1B_P167_F	5170	0.91373	0.94359	0.01325	TNFRSF1B_P167_F	2.3E+07	NM_001066.2	TNFRSF1B	7133	1	12149480	-167	Y	GGTACCCGAGTGCTGGGAGTGA[CG]CTGGAGGTATCGGCCAGCGAT	cg20587042
TNFRSF1B_E5_F	1331	0.96771	0.9605	0.13626	TNFRSF1B_E5_F	2.3E+07	NM_001066.2	TNFRSF1B	7133	1	12149652	5	Y	TCGCTTTAGTTCGAGGGCTAGCGAG[CG]CAGCGGAGCCTGGAGAGAAAGG	cg06978331
TP73_P945_F	2932	0.90572	0.89516	0.08019	TP73_P945_F	4885644	NM_005427.1	TP73	7161	1	3558044	-945	Y	GTGTGCTGCGCCGGTAGAGAGCTT[CG]GCCTGACCTAGCGCAGGTCTGG	cg21323562
TRIM29_E189_F	2952	0.94328	0.79102	0.0393	TRIM29_E189_F	1.7E+07	NM_012101.2	TRIM29	23650	11	119513884	189	Y	CAGGCTGCCACTGGGGCCCGA[CG]GGCTCCGGGCATCCCTGGCTTCTGGG	cg26414304
TRPM5_P721_F	2153	0.88281	0.87503	0.14548	TRPM5_P721_F	2.4E+07	NM_014555.2	TRPM5	29850	11	2401572	-721	N	GGCTCATGTCTCCAGCTGCC[CG]GTGAGTTCGGGCATCTCAGCCCT	cg03982381
IGFBP7_P297_F	1124	0.9499	0.91617	0.03955	TSC2_E140_F	1.1E+07	NM_000548.2	TSC2	7249	16	2038740	140	N	AGAGGGTAAACAGACGGAGTTTATCATCAC[CG]CGGAAATACTGAGAGTGAGTGA	cg01052512
TSP50_P137_F	2158	0.93517	0.94251	0.01257	TSP50_P137_F	3.2E+07	NM_013270.2	TSP50	29122	3	46734505	-137	Y	GCTCGTGTGTCTGACCCGCAAGGG[CG]CCCCTAGTGACAGCCCTCCCTATA	cg13403573
TSP50_E21_R	3987	0.94448	0.94389	0.06955	TSP50_E21_R	3.2E+07	NM_013270.2	TSP50	29122	3	46734347	21	Y	GGGTGGCAGCCGACTGCGTCTCT[CG]GAAGGCGCTCCCAGTGCCTCC	cg07522405
TUSC3_E29_R	3992	0.96571	0.95567	0.02158	TUSC3_E29_R	3E+07	NM_178234.1	TUSC3	7991	8	15442130	29	Y	CAGGTCTTCTCCCGTGAA[CG]GATGCTCTGTAGTCTCTCCTCTGCGTC	cg10249582
GALR1_P80_F	889	0.87988	0.79426	0.0251	USP29_E274_F	5.7E+07	NM_020903.2	USP29	57663	19	62323595	274	N	GATGACTTGAGCCTTGGGAT[CG]AGGGTGTAGTGAGGTATGATC	cg07368873
WNT1_P79_R	6115	0.88448	0.87282	0.07817	WNT1_P79_R	1.7E+07	NM_005430.2	WNT1	7471	12	47658424	-79	Y	CCATTGTCTGCGCCCTAAC[CG]GTGCGCCTGTGCCACAGTGCCTCC	cg08133093
WNT5A_P655_F	5397	0.93935	0.94768	0.04191	WNT5A_P655_F	4.1E+07	NM_003392.3	WNT5A	7474	3	55497026	-655	Y	CGTATCCCGTTCTTTCTCTTT[CG]GGTTGATCTCTTTTCCCGTTTT	cg19344602
WT1_E32_F	4207	0.92266	0.95388	0.01654	WT1_E32_F	6.6E+07	NM_024424.2	WT1	7490	11	32413631	32	Y	CGGAGAGCCCCGGGTGTGGG[CG]CTGCCTGAACCTCTTACCCAGCTG	cg20134916
XRCC1_P681_R	5328	0.92803	0.9665	0.03636	XRCC1_P681_R	5454171	NM_006297.1	XRCC1	7515	19	48772236	-681	Y	GGCTAGGACAGCAAATCTGAGTGAATTTT[CG]TAGTTTCGTAGGGAACCTGGATT	cg12562082
ZIM2_P22_F	2198	0.92699	0.94021	0.14451	ZIM2_P22_F	3.3E+07	NM_015363.3	ZIM2	23619	19	62043909	-22	Y	GCAGCTGCCAGACTTCTGCAC[CG]AGGTGCAGCTCGACGCCTCTGTCA	cg01034638
ZIM3_E203_F	4010	0.79602	0.95733	0.09578	ZIM3_E203_F	1.6E+07	NM_052882.1	ZIM3	114026	19	62348179	203	N	AAAACCTAATCGGCCCTTACC[CG]CTGATTCCGCATCATAATCCAGTCAA	cg22057816
CRIP1_P874_R	403	0.94593	0.90209	0.06005	ZMYND10_P329_F	3.8E+07	NM_015896.2	ZMYND10	51364	3	50358489	-329	Y	ATGGCTTCTTGGTCTCTATTTCTCG[CG]TCCCGGCTCCACTAGTTGGCTCTGA	cg16621790
ZNF264_P397_F	2225	0.80092	0.87251	0.04589	ZNF264_P397_F	5.6E+07	NM_003417.2	ZNF264	9422	19	62394284	-397	Y	GGGATGTGAAAGGGGTCAGT[CG]CCAGGCGAGCTGAGGACCCAGTTC	cg04803824

## **SUPPLEMENTARY METHODS**

### **Human cancer cell lines**

HCT-116 colon cancer cells and double DNMT1<sup>-/-</sup> and DNMT3B<sup>-/-</sup> (DKO) cells were grown as previously described<sup>1</sup>. HCT-116 cells were treated with 5-aza-2'-deoxycytidine (1  $\mu$ M) for 72 hours as previously described<sup>2</sup>. The DKO DNMT1/3B cell line was obtained by stably reintroducing the DNMT1 (cloned in a pCDNA3 vector (Life Technologies) with Zeocin resistance) and DNMT3B (cloned in a pIRES vector (Clontech) with Puromycin resistance) genes. The DNMT1 and DNMT3B levels of expression were checked by qRT-PCR (Supplementary Figure S1), and resembled those in the HCT-116 cell line. A western blot was performed to demonstrate that the observed expression came from the reintroduced DNMTs (Supplementary Figure S1). Nucleolin (Nucleolin Ab: Abcam, ab22758) was used as a control. Since the reintroduced DNMT1 and DNMT3B were marked with Flag and His-myc tags respectively, these antibodies (Flag Ab: Sigma-Aldrich, F3040; 6xHis Ab: Clontech, 631213) were used in the Western. The DKO DNMT1/3B cells were cultured in 1/400 Zeocin and 4.7 Puromycin concentrations.

### **DNA methylation analysis**

DNA methylation was determined by PCR analysis after bisulfite modification. Bisulfite genomic sequencing was carried out using the EZ DNA Methylation-Gold Kit<sup>TM</sup> (Zymo Research) according to the manufacturer's instructions. A minimum of eight colonies of each sequence and sample were automatically sequenced to determine the pattern of methylation, as previously described<sup>2</sup>. Bisulfite genomic-sequencing primers are shown in Supplementary Table S1.

### **Quantitative reverse-transcription PCR expression analysis**

RNA was isolated with TRIzol (Invitrogen) according to the manufacturer's instructions. Total RNA was then treated with DNase I (Ambion) and 1  $\mu$ g was retrotranscribed with Superscript II reverse transcriptase according to the manufacturer's instructions (Life Technologies). Real-time PCRs were performed in an Applied Biosystems 7900HT Fast Real-Time PCR System, using 40 ng of cDNA for each amplification. Expression values were normalized

with respect to *GAPDH* expression. Obtained values are expressed as fold change using the  $2^{-\Delta\Delta C_T}$  method<sup>3</sup>. Statistical significance was assessed with an ANOVA test (\*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$ ). Reverse-transcription PCR primers were designed in different exons to prevent DNA amplification (Supplementary Table S1).

### **Semi-quantitative reverse-transcription PCR expression analysis**

RNA was isolated with TRIzol (Invitrogen) according to the manufacturer's instructions. Total RNA was then treated with DNase I (Ambion) and 1  $\mu$ g was retrotranscribed with Superscript II reverse transcriptase according to the manufacturer's instructions (Life Technologies). PCR amplifications were run in 2% agarose gels. Reverse-transcription PCR primers were the same as in the - quantitative reverse-transcription PCR expression analysis experiments (Supplementary Table S1).

### **Doubling time assay**

Cell doubling time assay was performed as previously described<sup>4</sup>. The assay was performed as follows: the same cell number was plated in 6 well plates by triplicate and left to grow for 72 hours counting the cells every 24 hours. Cells were trypsinized and counted using a Neubauer chamber at 24, 48 and 72 hours. The doubling time was calculated as follows: (in hours) =  $h \cdot \ln(2) / \ln(c_2/c_1)$ .

### **MTT**

Cell viability was determined by the 3-(4, 5-dimethyl-2-thiazolyl)-2, 5-diphenyl-2H-tetrazolium bromide (MTT) assay as previously described<sup>5</sup>. Briefly, 800 cells were plated onto 96-well plates. Cells were cultured for 7 days. Each day a plate was analyzed by adding MTT to a final concentration of 0.1%. After 2.5 hours incubation (37°C, 5% CO<sub>2</sub>), the MTT metabolic product, formazan was dissolved in DMSO and absorbance was measured at 570 nm.

### **Colony formation assay**

Colony formation assays were performed as previously described<sup>5</sup>. In our colony formation experiments,  $2 \times 10^3$  and  $1 \times 10^3$  cells were plated in 6 well

plates by triplicate and left to grow for 7 days. After that, cells were fixed and stained with MTT reagent.

### **In Vivo Nude Mouse Tumor-Growth Assay**

In Vivo Nude Mouse Tumor-Growth Assays were performed as previously described<sup>6</sup>. Athymic nu/nu mice (Harlam), aged 4-5 weeks, were used for tumor xenografts. The animals were maintained in a sterile environment; their cages, food and bedding were sterilized by autoclaving. Mice were anesthetized with isoflurane and tumor cells were subcutaneously (s.c.) injected.  $3.5 \times 10^6$  of empty vector cell line (control) or 2 stably transfected cell clones expressing SMYD3int were diluted in PBS with Matrigel™ (2:1) (Beckton-Dickinson), and injected s.c. (n=32 for HCT-116 and n=34 for DKO and DKO DNMT1/3B). Tumor dimensions were measured using digital calipers. Tumor volume (in mm<sup>3</sup>) was estimated according to the formula  $V = D \times d^2 / 2$ , where  $D$  is the long axis and  $d$  the short axis of tumor. All animal experiments were approved by the Bellvitge Biomedical Research Institute (IDIBELL) Animal Care and Use Committee.

### **Extraction of nuclei**

Nuclei were obtained as previously described<sup>7</sup>. Growing cells were trypsinized and washed twice with cold phosphate buffer saline (PBS). Cells were resuspended in 1 ml of ice-cold RSB adding Nonidet P40 to a concentration of 1% and kept on ice for 10 min. After incubation cells were centrifuged for 5 min at 800  $g$  at 4°C. The supernatant was discarded and nuclei were resuspended in RSB plus NP40. Samples were centrifuged for 5 min at 800  $g$  at 4°C. Nuclei were washed with RSB without NP40 and centrifuged for 5 min at 5 000 rpm at 4°C. A wash of NaCl 0.4 M was used to remove most non-histone-bound proteins from chromatin. The supernatant was discarded and the nuclei were resuspended in the corresponding buffer.

### ***MspI* accessibility assay**

*MspI* accessibility assays were performed as previously described<sup>7</sup>. Nuclei were resuspended in 1x *MspI* buffer to give  $10^6$  nuclei per 400  $\mu$ l. Nuclei from each cell line were digested in a series of increasing *MspI* restriction enzyme (Roche

Molecular Biochemicals) concentrations (0 U/ml, 100 U/ml and 400 U/ml) at 37°C for 1 hour. Reactions were stopped by adding 100 µl of stop solution (20 mM Tris-HCl pH 7.5, 0.6 M NaCl, 1% SDS, 10 mM EDTA and 400 µg/ml proteinase K) and incubating at 37°C for 2 hours. DNA was purified by phenol/chloroform extraction and ethanol precipitation. Amplicons were amplified and quantified through real-time PCR in an Applied Biosystems 7900HT Fast Real-Time PCR System. Results were normalized with respect to a region that does not have any *MspI* restriction site. The results shown are the means of at least three independent experiments amplifying each sample in triplicate. Statistical significance was assessed with an ANOVA test (\* p<0.05, \*\* p<0.01, \*\*\* p<0.001). PCR primers are shown in Supplementary Table S1.

### ***In vitro* methylation footprinting**

We adapted the methyltransferase-based single-promoter analysis assay protocol<sup>8</sup> for use with methylated sequences. We substituted SssI methyltransferase for *MspI*, *HaeIII* and *AluI* methyltransferases (New England Biolabs). Extracted nuclei (~10<sup>6</sup>) were incubated for 30 min first with 60 U of *HaeIII*, then with 60 U of *MspI* and finally with 60 U of *AluI* methyltransferases. A 1x PBS wash was done between incubations and nuclei were resuspended in the corresponding buffer. The final reaction was stopped by adding 100 µl of stop solution (20 mM Tris-HCl pH 7.5, 0.6 M NaCl, 1% SDS, 10 mM EDTA and 400 µg/ml proteinase K) and incubating at 37°C for 2 hours. DNA was purified by phenol/chloroform extraction and ethanol precipitation. Naked DNA was used as a positive control to check the efficiency of the methyltransferases.

### **Time course with 5-aza-2'-deoxycytidine treatment**

Sixteen different time points (until 192 hours) have been analyzed: six time points with continuous Aza treatment and ten time points after Aza withdrawal at 72 hours. Every 12 hours DNA methylation bisulfite genomic sequencing analysis, RNA expression and *MspI* accessibility assays for three regions of the *HOXD1* and *RARB* promoter CpG islands were performed. Cells were never allowed to reach confluence. DNA methylation data and *MspI* accessibility assays data have been plotted in a single graph in order to facilitate interpretation. Absolute value of 1 in DNA methylation represents the maximum



demethylation percentage achieved with the Aza treatment after analyzing eight bisulfite sequencing clones. Absolute value of 1 in DNA accessibility represents the maximum DNA accessibility achieved with the Aza treatment analyzed by *MspI* accessibility assay. The Y axis of the graphs depicts these absolute scaled values.

### **Obtaining nucleosomal DNA**

To prepare mononucleosomal DNA,  $10^6$  nuclei were resuspended in 500  $\mu$ l MNase buffer. Then, 500 U/mL of MNase (Roche) were added and tubes were incubated for 0.5–10 min at 37°C. The reaction was stopped by adding EDTA to a final concentration of 20 mM and SDS to a final concentration of 1%. The suspension was centrifuged at 14,000 rpm for 15 min. The supernatant containing the nuclease digested nuclei was incubated with 0.1 mg/mL proteinase K overnight at 37°C. DNA was treated with RNase, extracted with phenol/chloroform, precipitated with ethanol, and finally resuspended in TE (10 mM Tris-HCl, 1 mM EDTA at pH 8.0). The DNA obtained was run on an agarose gel to produce a nucleosomal DNA ladder. The mononucleosomal band, corresponding to a 147 bp band, was recovered from the gel and the DNA was purified.

### **DNA methylation and nucleosome positioning profiling using bead arrays**

Methylation was assessed using Illumina Goldengate Methylation Arrays<sup>®</sup>, as previously described<sup>9</sup>. Illumina Goldengate Methylation Arrays<sup>®</sup>, include 1,505 CpG sites located from -1,500 bp to +500 bp around the transcription start sites of 808 selected genes (Golden-Gate DNA methylation BeadArray, Illumina, Inc.). The panel of genes includes oncogenes and tumor-suppressor genes, imprinted genes, genes involved in various signaling pathways, and those responsible for DNA repair, cell cycle control, metastasis, differentiation, and apoptosis. Sixty-nine percent ( $n = 1,044$ ) of the 1,505 CpG sites studied are located within a canonical CpG island, while 31% ( $n = 461$ ) are situated outside CpG islands. In this work, genomic DNA from HCT-116 and DKO cell lines was hybridized, wherein all the sequences with a difference of at least 70% between the two cell lines were considered to be hypermethylated in HCT-116 (genomic HCT116 hybridization signal – genomic DKO hybridization signal  $\geq 0.7$ ). We

next determined which of the methylated sequences were protected from MNase digestion due to nucleosome occupancy. The hybridization results of HCT116 mononucleosomic DNA were compared with DKO genomic DNA hybridization results, the sequences with an enrichment of 70% in the hybridization signal being considered to be protected (mononucleosomal HCT-116 hybridization signal – genomic DKO hybridization signal  $\geq 0.7$ ).

### **Quantitative chromatin immunoprecipitation**

Chromatin immunoprecipitation assays were performed as previously described<sup>10</sup>. Fixation was performed with 1% formaldehyde and sonication with Bioruptor (Diagenode, Liede, Belgium) was optimized to obtain 250–500 bp chromatin fragments. Each chromatin extract was immunoprecipitated with 2  $\mu$ g of total H3 (Rb Abcam1791). Non-related Rabbit IgG (Diagenode, kch-504-250) antibody was used as a negative control. Total DNA collected after sonication (input fraction) was used as positive control. Quantitative real-time PCR was performed in an Applied Biosystems 7900HT Fast Real-Time PCR System with specific primers for each of the analyzed promoters (Supplementary Table S1).

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