Figure S1

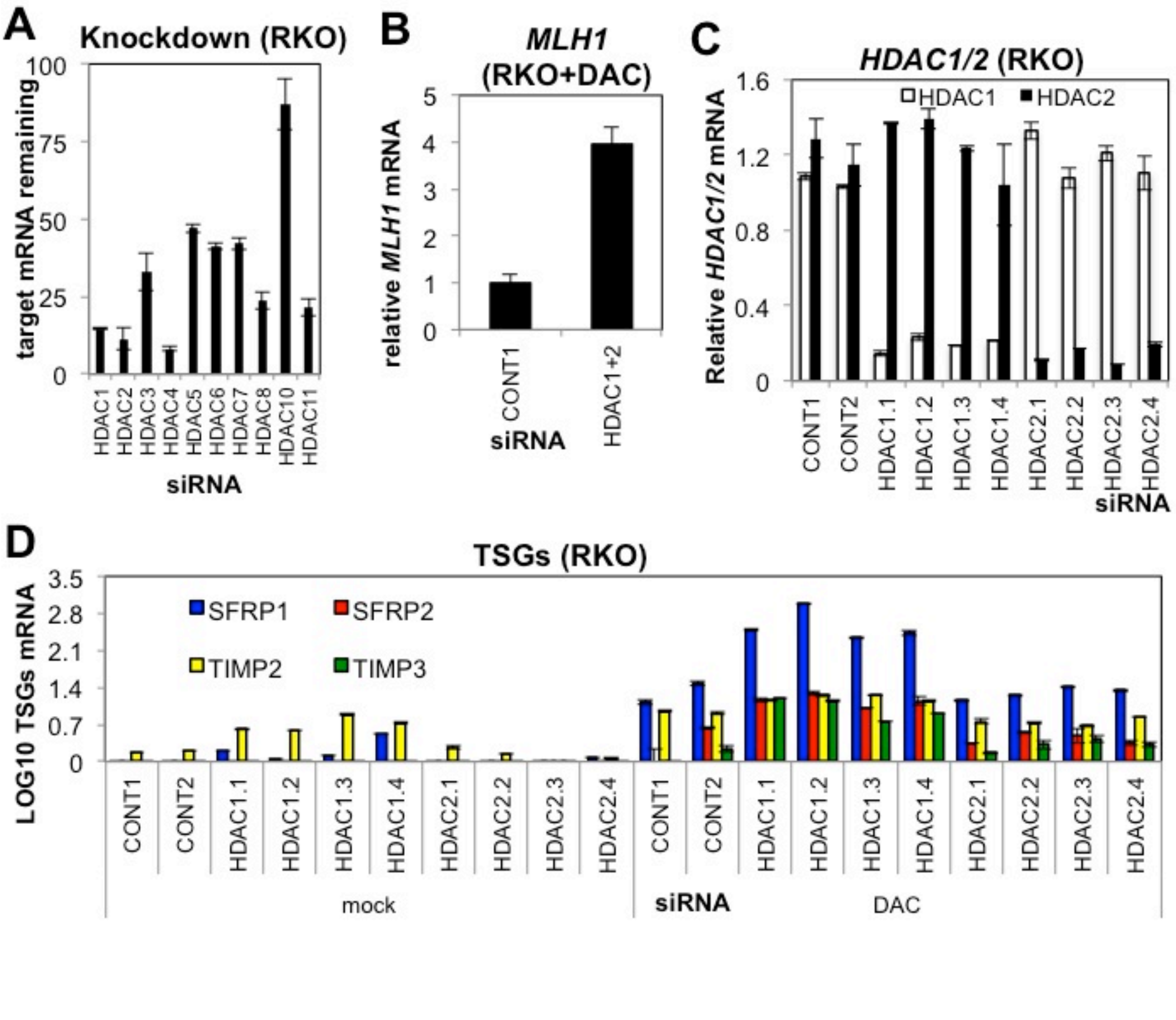

A
Knockdown (RKO)
target mRNA remaining
100
75
50
25
0
HDAC1
HDAC2
HDAC3
HDAC4
HDAC5
HDAC6
HDAC7
HDAC8
HDAC10
HDAC11
siRNA
B
MLH1
(RKO+DAC)
relative MLH1 mRNA
5
4
3
2
1
0
CONT1
HDAC1+2
siRNA
C
HDAC1/2 (RKO)
Relative HDAC1/2 mRNA
1.6
1.2
0.8
0.4
0
HDAC1
HDAC2
CONT1
CONT2
HDAC1.1
HDAC1.2
HDAC1.3
HDAC1.4
HDAC2.1
HDAC2.2
HDAC2.3
HDAC2.4
siRNA
D
TSGs (RKO)
LOG10 TSGs mRNA
3.5
2.8
2.1
1.4
0.7
0
SFRP1
SFRP2
TIMP2
TIMP3
CONT1
CONT2
HDAC1.1
HDAC1.2
HDAC1.3
HDAC1.4
HDAC2.1
HDAC2.2
HDAC2.3
HDAC2.4
mock
siRNA
DAC

Figure S2

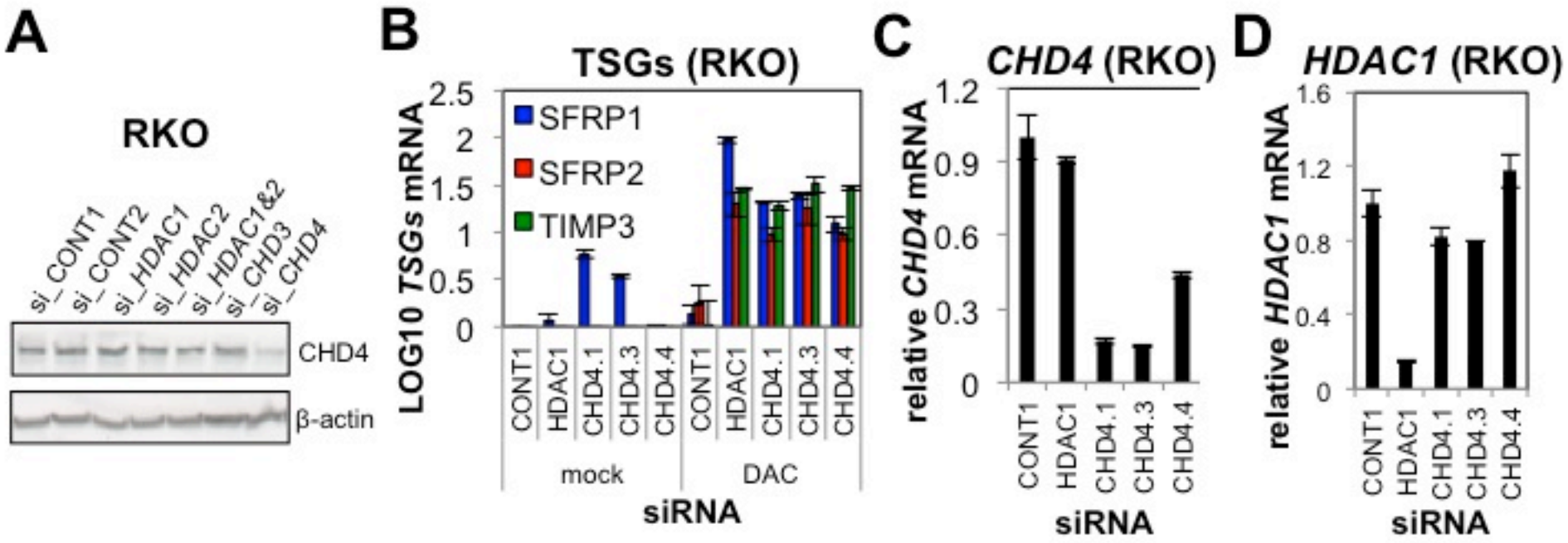

A
RKO
si_CONT1
si_CONT2
si_HDAC1
si_HDAC2
si_HDAC1&2
si_CHD3
si_CHD4
CHD4
β-actin
B
TSGs (RKO)
LOG10 TSGs mRNA
SFRP1
SFRP2
TIMP3
CONT1
HDAC1
CHD4.1
CHD4.3
CHD4.4
mock
DAC
siRNA
C
CHD4 (RKO)
relative CHD4 mRNA
siRNA
D
HDAC1 (RKO)
relative HDAC1 mRNA
siRNA

Figure S3

A

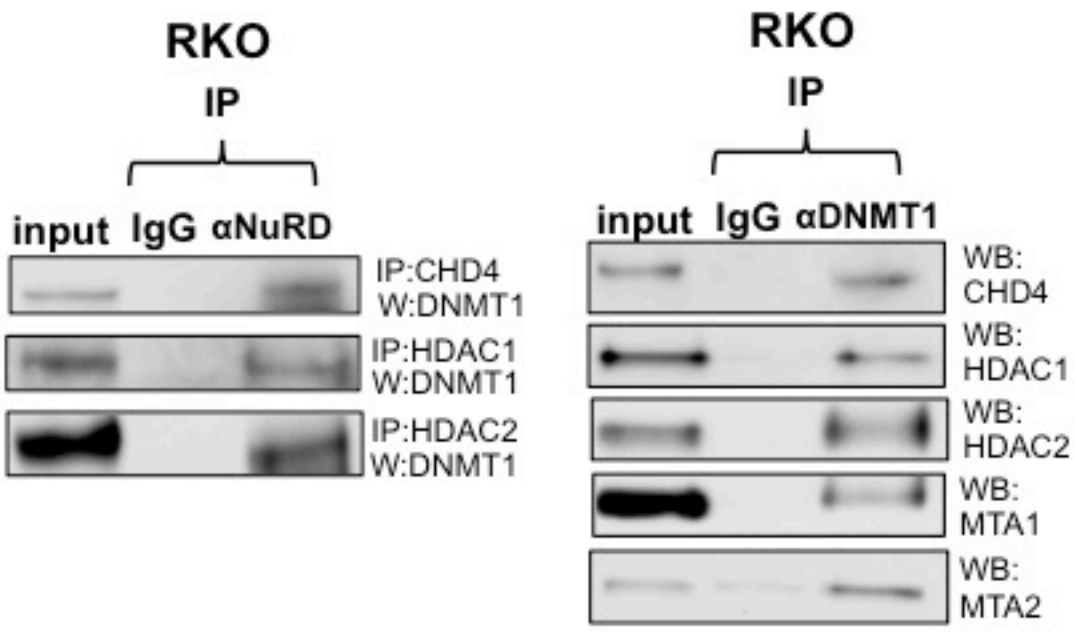

RKO
IP
input IgG αNuRD
IP:CHD4
W:DNMT1
IP:HDAC1
W:DNMT1
IP:HDAC2
W:DNMT1
RKO
IP
input IgG αDNMT1
WB:
CHD4
WB:
HDAC1
WB:
HDAC2
WB:
MTA1
WB:
MTA2

Figure S4

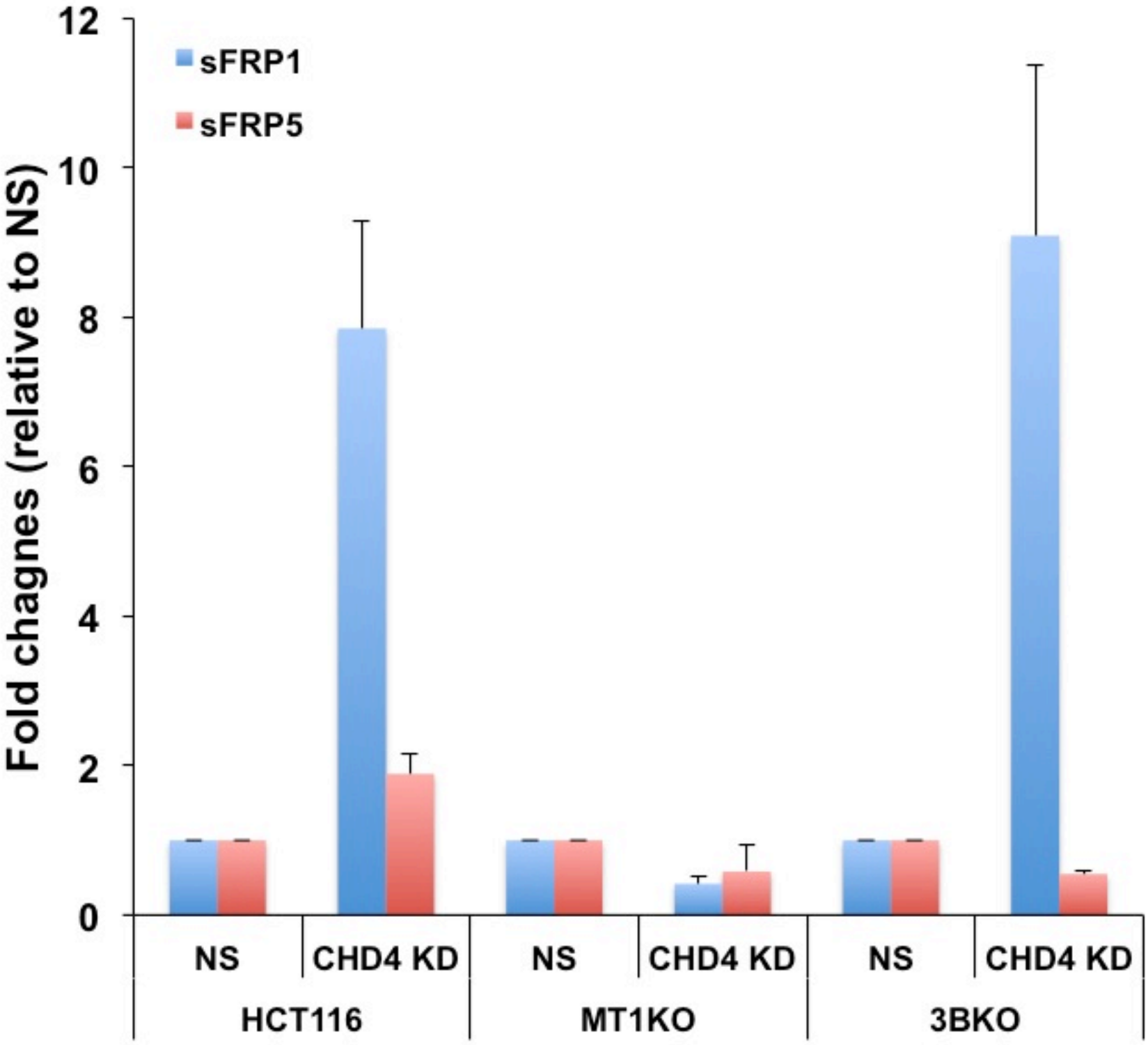
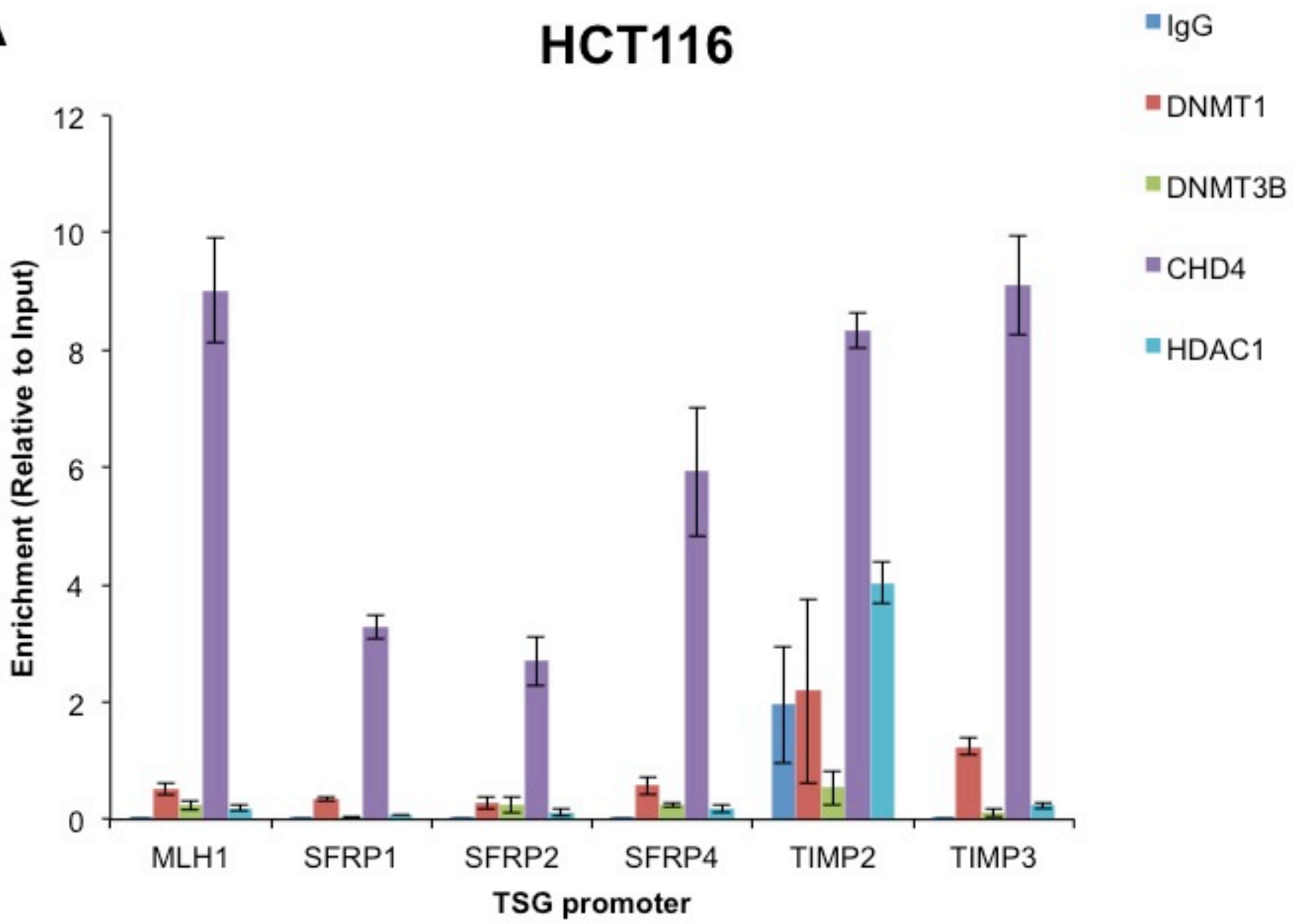

12
10
8
6
4
2
0
Fold chagnes (relative to NS)
sFRP1
sFRP5
NS
CHD4 KD
NS
CHD4 KD
NS
CHD4 KD
HCT116
MT1KO
3BKO

FIGURE S5

A


HCT116
IgG
DNMT1
DNMT3B
CHD4
HDAC1
Enrichment (Relative to Input)
12
10
8
6
4
2
0
MLH1
SFRP1
SFRP2
SFRP4
TIMP2
TIMP3
TSG promoter

B

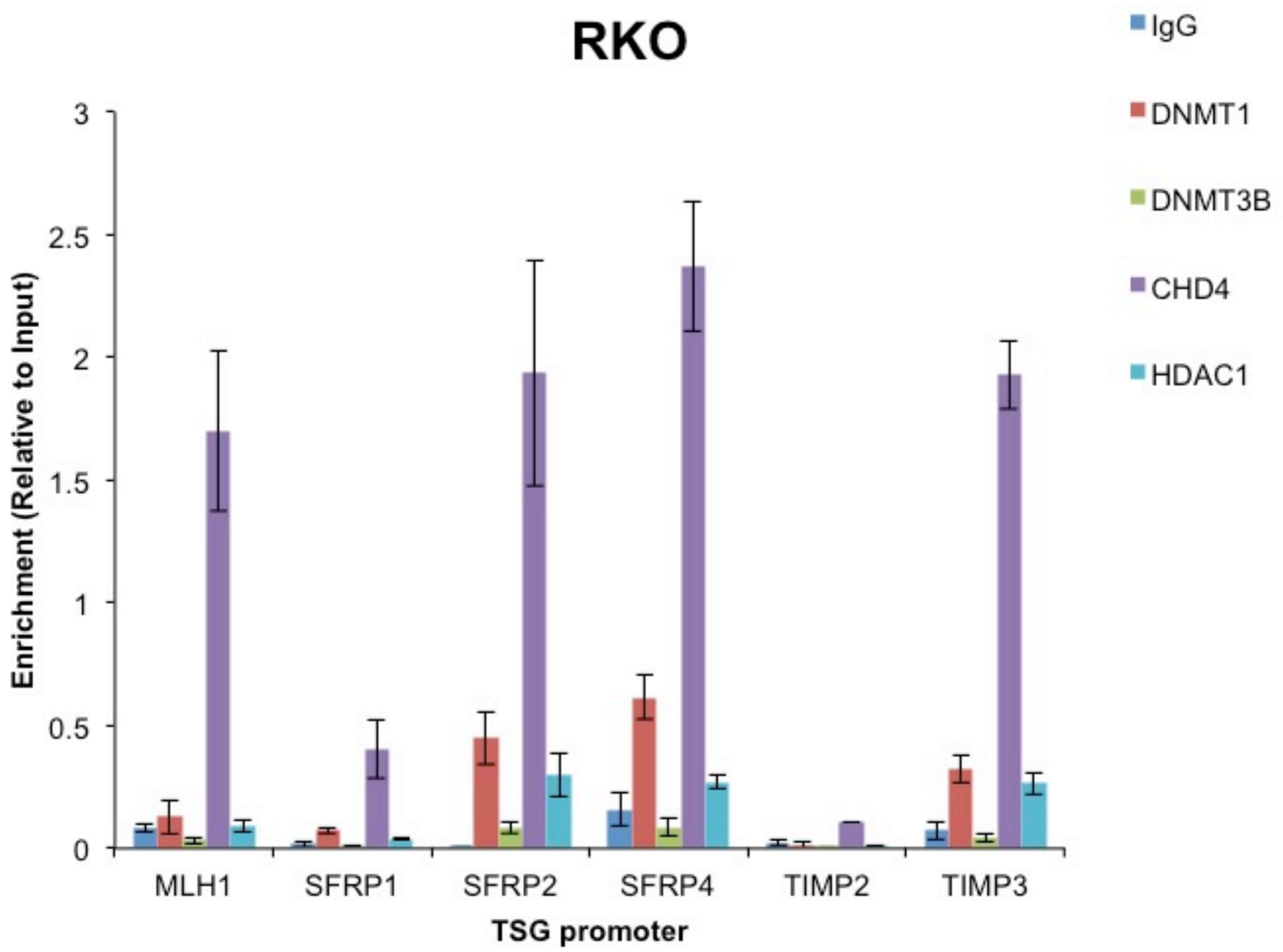
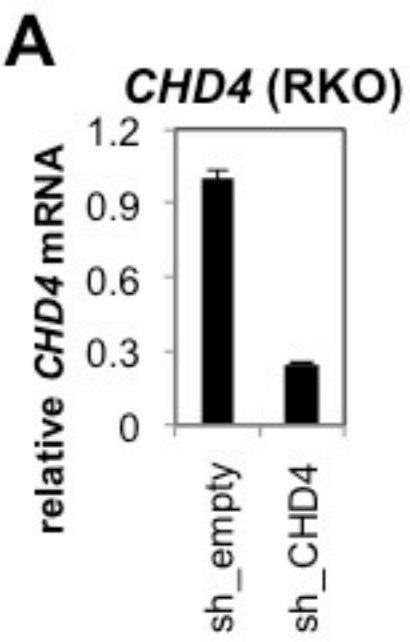
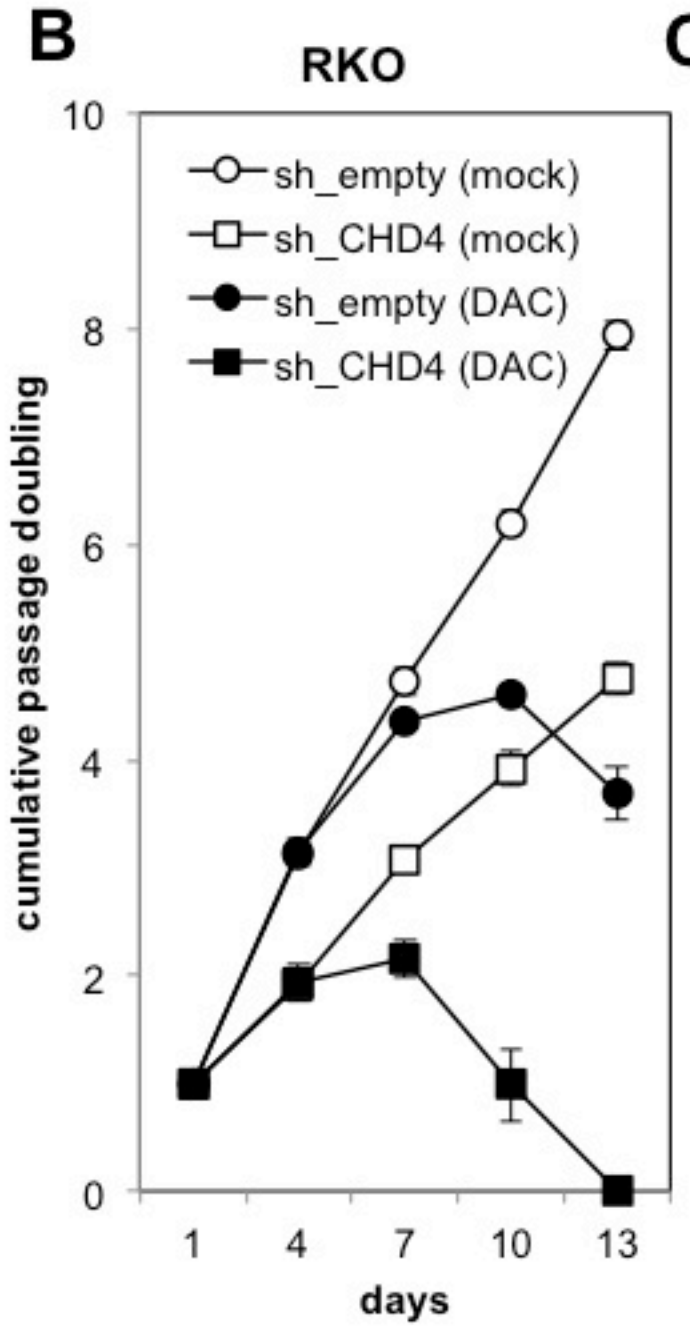
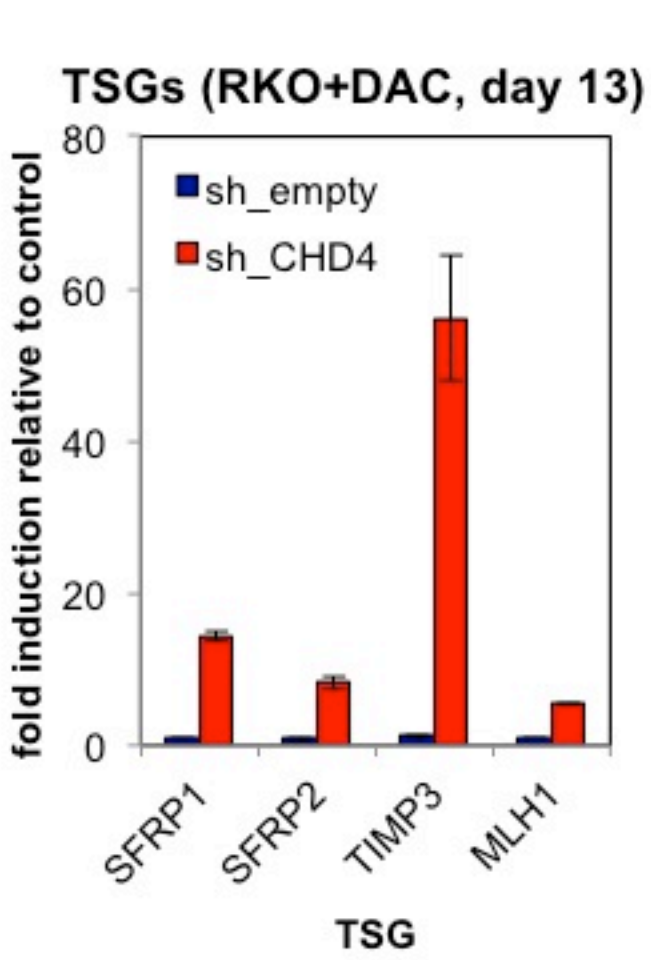
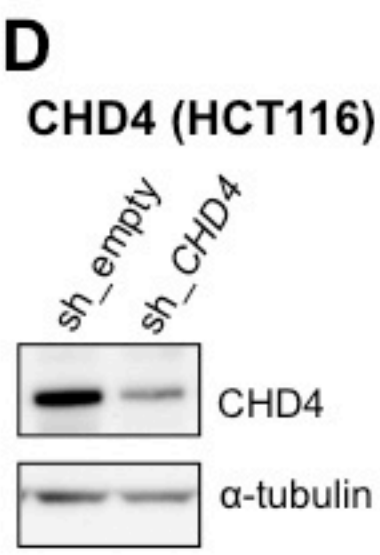

RKO
IgG
DNMT1
DNMT3B
CHD4
HDAC1
Enrichment (Relative to Input)
3
2.5
2
1.5
1
0.5
0
MLH1
SFRP1
SFRP2
SFRP4
TIMP2
TIMP3
TSG promoter

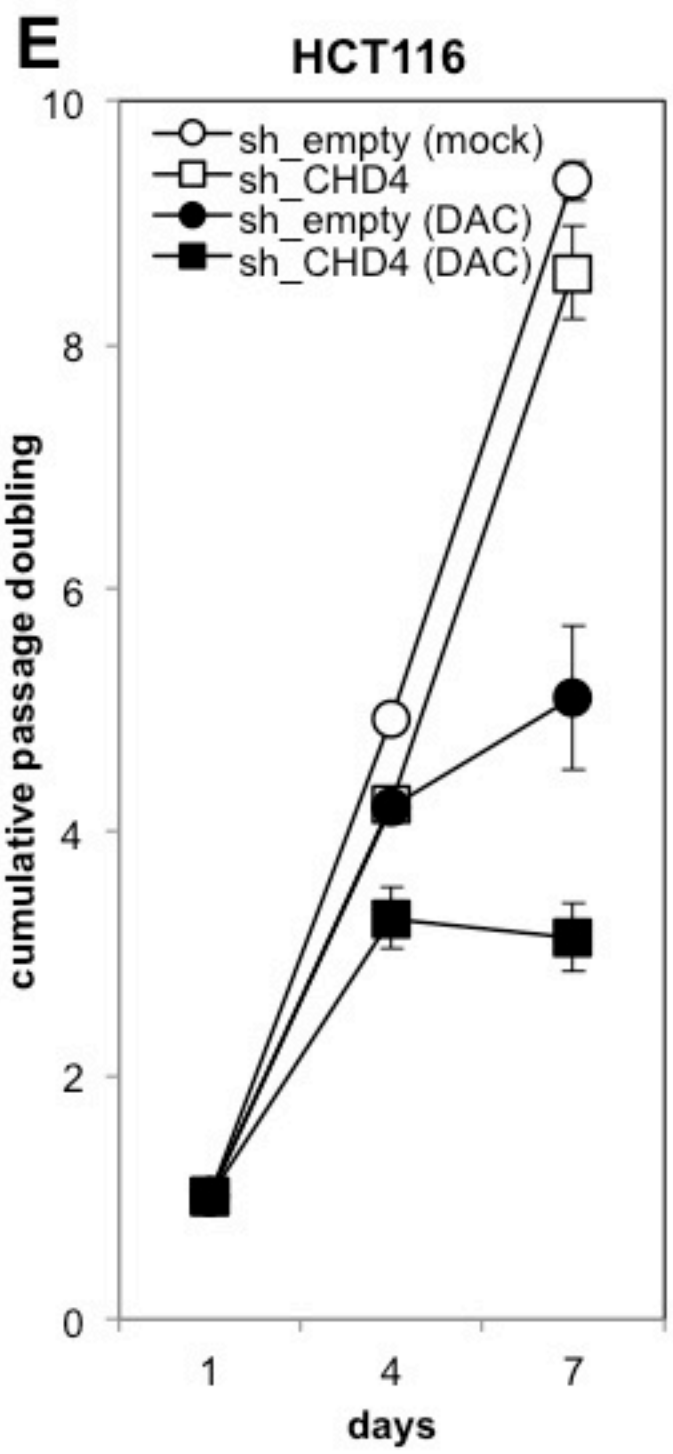
FIGURE S6

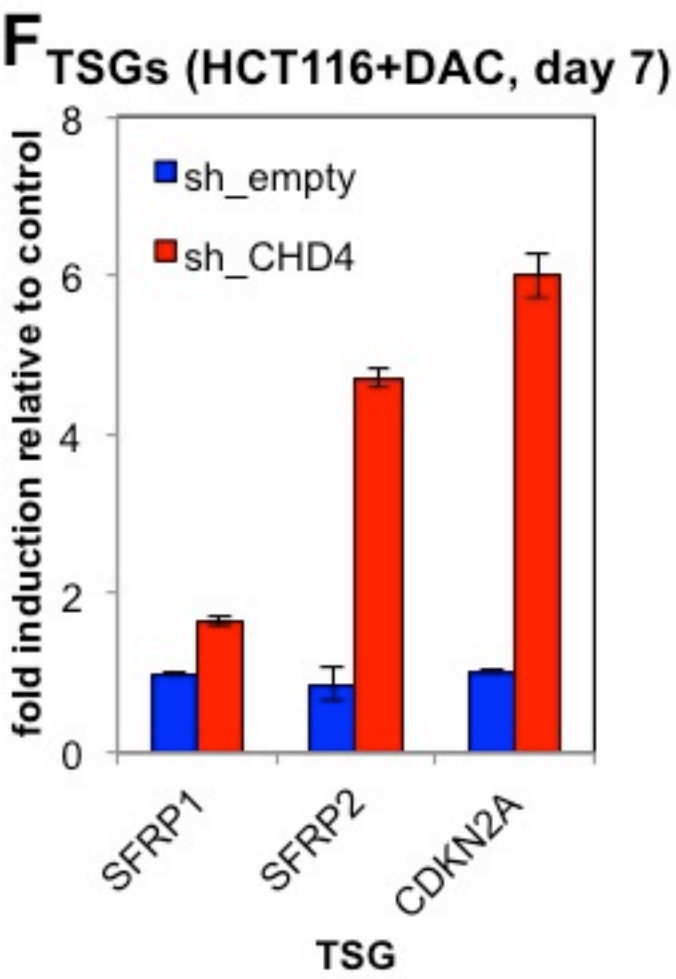

A
CHD4 (RKO)
relative CHD4 mRNA
1.2
0.9
0.6
0.3
0
sh_empty
sh_CHD4


B
RKO
cumulative passage doubling
10
8
6
4
2
0
sh_empty (mock)
sh_CHD4 (mock)
sh_empty (DAC)
sh_CHD4 (DAC)
1
4
7
10
13
days


C
TSGs (RKO+DAC, day 13)
fold induction relative to control
80
60
40
20
0
sh_empty
sh_CHD4
SFRP1
SFRP2
TIMP3
MLH1
TSG


D
CHD4 (HCT116)
sh_empty
sh_CHD4
CHD4
α-tubulin


E
HCT116
cumulative passage doubling
10
8
6
4
2
0
sh_empty (mock)
sh_CHD4
sh_empty (DAC)
sh_CHD4 (DAC)
1
4
7
days


F
TSGs (HCT116+DAC, day 7)
fold induction relative to control
8
6
4
2
0
sh_empty
sh_CHD4
SFRP1
SFRP2
CDKN2A
TSG

ensembl_gene_id	hgnc_symbol
ENSG00000006611	ACSBG1
ENSG00000007350	ADAMTS1
ENSG00000010319	ADAMTS2
ENSG00000011201	ALDH1L1
ENSG00000012779	ALOX5
ENSG00000028137	ANKRD36BP2
ENSG00000048545	ARHGEF25
ENSG00000054219	ATP1B2
ENSG00000054356	C14orf132
ENSG00000061337	C1orf61
ENSG00000064300	C5orf47
ENSG00000073910	C5orf58
ENSG00000075043	C7orf52
ENSG00000080709	CA9
ENSG00000087116	CACNG7
ENSG00000095752	CALY
ENSG00000100593	CAPN12
ENSG00000101198	CD248
ENSG00000101204	CD93
ENSG00000101871	CHRNA4
ENSG00000102287	COL6A2
ENSG00000103740	COX6B2
ENSG00000104044	CREB3L1
ENSG00000104332	CXorf48
ENSG00000105122	DPP6
ENSG00000105605	DPYSL3
ENSG00000105696	DPYSL5
ENSG00000107159	EHF
ENSG00000108823	ENOX1
ENSG00000111452	EPHB3
ENSG00000113657	EVL
ENSG00000115590	FAM127C
ENSG00000116962	FAM9A
ENSG00000120658	FAM9C
ENSG00000125462	FGA
ENSG00000125810	FRY
ENSG00000129244	GAB4
ENSG00000129455	GABRE
ENSG00000130035	GABRQ
ENSG00000130226	GALNT8

ENSG00000130508	GBA3
ENSG00000130592	GBP5
ENSG00000130643	GIPC3
ENSG00000131721	GNG4
ENSG00000131771	GPR133
ENSG00000133116	GPR45
ENSG00000134201	GRASP
ENSG00000135373	GREM1
ENSG00000135973	GRIK4
ENSG00000137285	GRIN2A
ENSG00000140538	GSTM5
ENSG00000141750	GUCA1A
ENSG00000142173	HEYL
ENSG00000143867	HKDC1
ENSG00000144908	HMX1
ENSG00000145832	IGF2
ENSG00000147402	IL11
ENSG00000149131	IL1R2
ENSG00000149403	IL1RAPL1
ENSG00000154451	IL24
ENSG00000154734	IRX1
ENSG00000156510	ISM2
ENSG00000157570	ITGB2
ENSG00000157613	ITGBL1
ENSG00000157851	KAL1
ENSG00000160191	KCNN2
ENSG00000160255	KCNQ2
ENSG00000160471	KCNS3
ENSG00000160472	KL
ENSG00000161835	KLK8
ENSG00000162738	LCK
ENSG00000162892	LGI3
ENSG00000163909	LSP1
ENSG00000163914	LY75
ENSG00000164736	LZTS1
ENSG00000166402	MAF
ENSG00000166501	MID1
ENSG00000166532	MRGPRF
ENSG00000166923	MYBPHL
ENSG00000167011	NBEA
ENSG00000167207	NCRNA00226

ENSG00000167244	NGFR
ENSG00000168243	NID1
ENSG00000168481	NKAIN4
ENSG00000168930	NMUR1
ENSG00000169302	NOD2
ENSG00000169306	NTRK3
ENSG00000169551	NUP62CL
ENSG00000170549	OCA2
ENSG00000170745	OSR1
ENSG00000171227	PCP4L1
ENSG00000171560	PDE9A
ENSG00000171596	PLK5
ENSG00000172915	PPP1R1B
ENSG00000172935	PRKCB
ENSG00000174807	PSG9
ENSG00000176887	PTPRN
ENSG00000178573	PXDN
ENSG00000178726	RASAL3
ENSG00000179855	RFPL4A
ENSG00000180739	RHO
ENSG00000181291	RHOXF2
ENSG00000182472	RIMKLB
ENSG00000182580	RTN4RL1
ENSG00000182866	S1PR3
ENSG00000183160	S1PR5
ENSG00000183304	SEMA3G
ENSG00000183439	SERPING1
ENSG00000183454	SFRP1
ENSG00000183668	SGCA
ENSG00000184905	SLC25A48
ENSG00000185037	SMPD4P1
ENSG00000185056	SNAI1P1
ENSG00000185177	SNX18P15
ENSG00000185924	SOX11
ENSG00000185988	SOX17
ENSG00000187268	STAC2
ENSG00000196405	STK32A
ENSG00000196593	TCEAL2
ENSG00000197123	THBD
ENSG00000198088	TKTL1
ENSG00000198542	TMEM119

ENSG00000204603	TMEM132E
ENSG00000212747	TMEM158
ENSG00000213694	TMEM190
ENSG00000214049	TMEM37
ENSG00000215568	TMEM59L
ENSG00000215612	TNFRSF1B
ENSG00000218014	TRIM49
ENSG00000221180	TRIM61
ENSG00000221986	TSPAN18
ENSG00000223553	TUB
ENSG00000223638	TUBB2B
ENSG00000223831	UCA1
ENSG00000223977	USH1C
ENSG00000225015	VANGL2
ENSG00000226364	VN2R19P
ENSG00000227051	ZNF479
ENSG00000229084	ZNF679
ENSG00000230006	SFRP2
ENSG00000231254	
ENSG00000234062	
ENSG00000234511	
ENSG00000235974	
ENSG00000236345	
ENSG00000236516	
ENSG00000236669	
ENSG00000237194	
ENSG00000237271	
ENSG00000237412	
ENSG00000240771	
ENSG00000248485	
ENSG00000249790	
ENSG00000249948	
ENSG00000249992	
ENSG00000251127	
ENSG00000253315	
ENSG00000253595	
ENSG00000254533	
ENSG00000258732	
ENSG00000145423	

Legend of supporting information

Figure S1 Validation of HDAC1 as a repressor of TSGs.

(A) Knockdown efficiency of the HDAC siRNA library. The knockdown abilities of the siRNA pools targeting *HDAC1-11* are depicted as the relative mRNA remaining compared to scrambled siRNA pools (see also Figure 1A). *HDAC9* is not expressed in RKO cells. (B) *HDAC1* and *HDAC2* siRNA pools enhance DAC-induced reactivation of *MLH1*. RKO cells were transfected with scrambled siRNA or a siRNA pools targeting *MLH1*, split and then treated with or without 100nM DAC. *MLH1* expression was determined by QRT-PCR and normalized to control. (C-D) All four *HDAC1* siRNAs induce reactivation of TSGs in combination with DAC and induce knockdown of *HDAC1*. RKO cells were transfected with scrambled or deconvoluted *HDAC1* or *HDAC2* siRNA pools, split and treated with or without 1μM DAC. Expression of indicated TSGs (C), *HDAC1* and 2 (D) was determined by QRT-PCR. TSG QRT-PCR values were Log10 transformed, *HDAC1* and *2* QRT-PCR values were normalized to control.

Figure S2 HDAC1 requires the NuRD complex for silencing of TSGs.

(A) *CHD4* siRNA pools induce depletion of CHD4. RKO cells were transfected with scrambled (CONT1 and 2), *HDAC1, HDAC2, CHD3* and *CHD4* siRNA pools. CHD4 protein expression was analyzed by western blotting, ß-actin serves as a loading control. (B-D) Three *CHD4* siRNAs induce knockdown of *CHD4* but not *HDAC1* and reactivate TSGs expression in combination with DAC. RKO cells were transfected with scrambled (CONT1), and deconvoluted *CHD4* siRNA pools, split and treated with or without 1μM DAC. Expression of indicated TSGs (B), *CHD4* (C) and *HDAC1* (D) was determined by QRT-PCR. TSG QRT-PCR values were Log10 transformed, *CHD4* and *HDAC1* QRT-PCR values were normalized to control. Error bars denote SD.

Figure S3 DNMT1 and NuRD physically interact in RKO cells.

DNMT1 interacts with the NuRD complex in RKO cells. Nuclear extracts from RKO cells were immunoprecipitated with antibodies against either NuRD complex subunits (left) or DNMT1 (right). Immunoprecipitates were immunoblotted using the indicated antibodies.

Figure S4 Silencing of *SFRP1* and *SFRP5* in HCT116 cells does not rely on functional cooperation between CHD4 and either DNMT1 or DNMT3B.

Wild-type, *DNMT1* hypomorphic or *DNMT3B*-/- HCT116 cells were transduced with an empty vector or a functional shRNA targeting *CHD4*. Expression of *SFRP1* and *SFRP5* was analyzed by QRT-PCR and is represented as fold induction over empty vector. Error bars denote standard deviation (SD).

Figure S5 DNMTs and NuRD occupy promoters of TSGs.

(A) DNMT1, DNMT3B, HDAC1 and CHD4 associate with the proximal promoters of TSGs in HCT116 cells. (B) DNMT1, DNMT3B, HDAC1 and CHD4 associate with the proximal promoters of TSGs in RKO cells. Results are presented as percentage of input. Rabbit IgG served as a negative control. Error bars denote SD.

Figure S6 DAC and knockdown of *CHD4* synergize in cell death induction, in correlation with reactivation of TSGs.

(A) *CHD4* shRNA induces depletion of *CHD4*. RKO cells were transduced with an empty vector or an shRNA targeting *CHD4*. *CHD4* knockdown was verified by examining *CHD4* mRNA levels by QRT-PCR. Error bars denote SD. (B) Knockdown of *CHD4* sensitizes RKO cells to DAC treatment. RKO cells expressing empty vector or *CHD4* shRNA were seeded for proliferation assays according to the 3T3 protocol in absence of drug or presence of 1μM DAC. Error bars denote SD. (C) Synergistic reactivation of TSGs in cells treated with DAC and depleted for *CHD4*. Expression of indicated TSGs were examined by QRT-PCR on DAC treated samples harvested on day 13 of the proliferation assay. Values are represented as fold

induction over empty vector. Error bars denote SD. (D) *CHD4* shRNA induces depletion of *CHD4*. HCT116 cells were transduced with an empty vector or an shRNA targeting *CHD4*. *CHD4* knockdown was verified by western blotting, α-tubulin serves as a loading control. (E) Knockdown of *CHD4* sensitizes HCT116 cells to DAC treatment. HCT116 cells expressing empty vector or *CHD4* shRNA were seeded for proliferation assays according to the 3T3 protocol in absence of drug or presence of 1μM DAC. Error bars denote SD. (F) Synergistic reactivation of TSGs in cells treated with DAC and depleted for *CHD4*. Expression of indicated TSGs were examined by QRT-PCR on DAC treated samples harvested on day 7 of the proliferation assay. Values are represented as fold induction over empty vector. Error bars denote SD.

Table S1 NuRD complex components and known DNMT1 interacting partners identified by tandem mass spectrometry from the DNMT1 immunoprecipitate of HCT116 cells.

Endogenous DNMT1 was immunoprecipitated from nuclear extracts of HCT116 cells and captured by protein A/G beads. Immunoprecipitates were extracted from protein A/G beads and resolved on SDS-PAGE. Protein gel bands were cut and in-gel digested with trypsin. Extracted peptides were analyzed by reversed-phase nanoflow LC-tandem mass spectrometry. The raw MS/MS data were searched using the SEQUEST cluster against a human IPI proteome database. M*, methionine oxidation; C#, cysteine carboxyamidomethylation; MH+, monoisotopic mass of peptide with one proton; DeltaM (ppm), mass measurement error in terms of ppm; z, charge of peptide molecular ions; P (pro), probability for proteins; P (pep), probability for peptides; XC, cross-correlation score; DeltaCn, the difference of XCs between the top-matched peptide and second top-matched peptide.

Table S2 List of oligonucleotide sequences used in this study.

Table S3 List of antibodies used in this study.

Dataset S1 List of genes reactivated by DNMT inhibition and depletion of *HDAC1* or *CHD4*. Transcripts enhanced in DAC-induced reactivation by *CHD4* or *HDAC1* knockdown (see methods for cut-off criteria). (A) Transcripts enhanced in DAC-induced reactivation by *HDAC1* knockdown. (B) Transcripts enhanced in DAC-induced reactivation by *CHD4* knockdown. (C) Transcripts enhanced in DAC-induced reactivation by both *HDAC1* and *CHD4* knockdown: 40% of target genes overlap. Positive control TSGs and WNT inhibitors are highlighted in yellow.

Supplementary Methods:

Chromatin immunoprecipitation (ChIP)

Both the Baylin Lab and the Bernards lab obtained similar NuRD and DNMT ChIP results with different protocols. In the Bernards Lab, ChIP experiments were performed using the SimpleChIP enzymatic chromatin IP kit (Cell signaling technologies) using the manufacturer's instructions with some minor adjustments. 10^7 RKO cells were fixed with 1% formaldehyde (Merck) for 15' room temperature (RT) at a rotating platform. Nuclei were incubated with 7ul micrococcal nuclease for 30' at 37 C. Nuclei were sheared with the Diagenode Biorupter using the low output setting and 15 cycles (30s on, 30s off) of sonication. The ChIP protocol in the Baylin Lab was described previously with minor adjustments in the washing steps(49). For DNMT1 ChIP, wash 5 times with low salt wash buffer; for DNMT3B ChIP, first wash with low salt wash buffer for 4 times, then wash with high salt wash buffer twice; for HDAC1 and CHD4 ChIP, first wash with low salt wash buffer for 4 times, then wash with high salt wash buffer once.

Re-ChIP

The re-ChIP protocol is described previously with modification in the first ChIP elution step (Truax and Greer, Methods Mol. Biol, 2012, 809:175-88). For the DNMT3B re-ChIP assay, DNMT3B antibody immunogen peptide (ENKTRRRTADDSATS) was used to elute the chromatin complex from the magnetic beads after the first ChIP. For DNMT1 ChIP, as the elution efficiency of Sigma DNMT1 antibody (D4692) immunogen peptide is very low, we first ChIP FLAG-DNMT1 in a FLAG-DNMT1 stable cell line in HCT116 cells (49) with anti-FLAG magnetic beads (Sigma) and then elute with FLAG peptide (Sigma). For peptide elution, first dissolve peptide in 0.5 M Tris HCl (pH 7.5) with 1 M NaCl at a concentration of 25 mg/ml. Dilute 5-fold with water to prepare a peptide stock solution containing 5 mg/ml of immunogen peptide. For ChIP elution, add 3 ul of 5 mg/ml of immunogen peptide stock solution to 100 ul of TBS (50 mM Tris pH 7.5, 150 mM NaCl) to reach 150 ng/ml final concentration, then add it to chromatin-bound magnetic beads and rotate at 4C for 1 hour for elution.

Table S1. NuRD complex components identified by tandem mass spectrometry from the DNMT1 immunoprecipitate of HCT116 cells.

Endogenous DNMT1 was immunoprecipitated from nuclear extracts of HCT116 cells and captured by protein A/G beads. Immunoprecipitates were extracted from protein A/G beads and resolved on SDS-PAGE. Protein gel bands were cut and in-gel digested with trypsin. Extracted peptides were analyzed by reversed-phase nanoflow LC-tandem mass spectrometry. The raw MS/MS data were searched using the SEQUEST cluster against a human IPI proteome database. M*, methionine oxidation; C#, cysteine carboxyamidomethylation; MH+, monoisotopic mass of peptide with one proton; DeltaM (ppm), mass measurement error in terms of ppm; z, charge of peptide molecular ions; P (pro), probability for proteins; P (pep), probability for peptides; XC, cross-correlation score; DeltaCn, the difference of XCs between the top-matched peptide and second top-matched peptide.

Gene	**Protein**				**P (pro)**	**Score**	
Scan #	**Peptide**	**MH+**	**DeltaM (ppm)**	**z**	**P (pep)**	**XC**	**DeltaCn**
CHD4	**Chromodomain-helicase-DNA-binding protein 4**				**3.38E-09**	**220.23**	
674	K.FAEM*EER.F	927.3877	-1.4229	2	3.15E-03	2.68	0.36
802	K.FAEM*EER.F	927.3877	-1.4229	2	8.97E-03	2.53	0.44
949	R.KEEEEEDDDDDDSKEPK.S	2051.8047	-0.6034	3	7.31E-08	4.13	0.88
973	K.QVNYNDGSQEDR.D	1424.6037	2.0632	2	5.56E-06	2.75	0.69
997	R.TEEPM*ETEPK.G	1206.5195	-0.6103	2	1.60E-03	2.73	0.58
1126	K.ERTEEPM*ETEPK.G	1491.6632	0.0609	2	9.23E-03	2.96	0.56
1127	K.ERTEEPM*ETEPK.G	1491.6632	0.0609	2	6.57E-04	3.04	0.50
1178	R.EEEM*GEEEEVER.E	1510.5850	-0.2196	2	1.12E-06	3.09	0.66
1179	R.EEEM*GEEEEVER.E	1510.5850	-0.2196	2	3.20E-07	3.74	0.69
1180	R.EEEM*GEEEEVER.E	1510.5850	-0.2196	2	1.34E-06	3.86	0.68
1283	R.IDGGITGNM*R.Q	1049.5044	-0.4439	2	3.01E-06	3.23	0.53
1284	R.VELSPM*QK.K	947.4866	-0.0903	2	1.83E-03	2.63	0.35
1286	R.IDGGITGNM*R.Q	1049.5044	-0.4439	2	5.53E-06	3.49	0.53
1376	K.GAADVEKVEEK.S	1174.5950	-0.3034	2	7.30E-04	3.80	0.43
1442	K.EVM*LQNGETPK.D	1261.6093	0.5978	2	8.72E-04	2.57	0.36
1444	K.EVM*LQNGETPK.D	1261.6093	0.5978	2	7.15E-03	3.03	0.36
1501	K.VAQYVVR.E	834.4832	1.0992	1	1.80E-03	2.04	0.43
1532	R.APEPTPQQVAQQQ.-	1421.7019	-0.0727	2	9.04E-04	3.17	0.53
1534	R.APEPTPQQVAQQQ.-	1421.7019	-0.0727	2	2.44E-04	3.66	0.55
1618	R.WQDIQNDPR.Y	1171.5491	-0.8878	2	1.34E-07	3.13	0.45
1619	R.WQDIQNDPR.Y	1171.5491	-0.8878	2	2.10E-06	3.48	0.46
2355	K.QLEELLSDM*K.A	1221.6031	0.3541	2	1.55E-03	2.70	0.35

2357	K.QLEELLSDM*K.A	1221.6031	0.3541	2	5.45E-04	2.89	0.34
2493	R.ENEFSFEDNAIR.G	1470.6496	-0.5671	2	6.03E-07	3.50	0.63
2494	R.ENEFSFEDNAIR.G	1470.6496	-0.5671	2	3.26E-07	3.82	0.58
2635	K.AFLNAIM*R.Y	951.5080	-0.6471	2	9.79E-05	2.84	0.35
2637	K.AFLNAIM*R.Y	951.5080	-0.6471	2	4.07E-03	2.74	0.30
2700	K.SAIDLTPIVVEDK.E	1399.7679	0.1619	2	3.38E-09	3.68	0.53
2703	K.SAIDLTPIVVEDK.E	1399.7679	0.1619	2	9.24E-08	3.52	0.50
2755	K.AFLNAIM*R.Y	951.5080	-0.6471	2	7.04E-04	2.72	0.28
2829	R.VGGNIEVLGFNAR.Q	1345.7223	0.0468	2	6.54E-04	4.12	0.54
2904	R.VGGNIEVLGFNAR.Q	1345.7223	-0.2253	2	2.13E-04	3.60	0.54
3006	R.IGVM*SLIR.K	904.5284	-0.1579	2	5.52E-03	2.58	0.39
3367	K.LLEQALVIEEQLR.R	1553.8897	1.0755	2	7.83E-09	4.52	0.50
3371	K.LLEQALVIEEQLR.R	1553.8897	0.9969	2	7.45E-09	3.93	0.49
3456	K.LLEQALVIEEQLR.R	1553.8897	0.6827	2	3.01E-06	3.80	0.54
3579	R.GGGNQVSLLNVVM*DLK.K	1659.8734	0.3848	2	9.76E-06	4.09	0.63
3580	R.GGGNQVSLLNVVM*DLK.K	1659.8734	0.3848	2	8.28E-06	3.97	0.63
3694	R.GGGNQVSLLNVVM*DLK.K	1659.8734	0.3113	2	7.15E-07	4.05	0.58
4060	K.GPFLVSAPLSTIINWER.E	1900.0327	0.6702	2	4.95E-08	3.27	0.70
MTA1	**Metastasis-associated protein MTA1**				**1.97E-07**	**70.20**	
1170	R.ALDC#SSSVR.Q	994.4622	0.9058	2	7.59E-04	2.93	0.41
1846	K.NIYDISK.A	852.4462	1.9421	1	6.81E-03	1.89	0.07
2503	R.LPEASQSPLVLK.Q	1281.7413	0.6509	2	4.14E-06	3.65	0.38
2711	K.C#SVTLLNETESLK.S	1493.7516	2.2391	2	1.97E-07	3.73	0.21
2949	R.YQADITDLLK.E	1179.6256	1.8250	2	2.54E-05	2.94	0.18
2968	K.SVSSVLSSLTPAK.V	1275.7155	1.8524	2	3.06E-07	3.24	0.46
3314	R.DISSTLIALADK.H	1246.6889	2.1393	2	1.31E-05	3.08	0.69
3316	R.DISSTLIALADK.H	1246.6889	2.1393	2	5.88E-05	4.03	0.68
GATAD2A	**Transcriptional repressor p66-alpha**				**5.05E-10**	**60.21**	
845	R.ATEATAM*AM*GR.G	1141.4976	1.8057	2	4.11E-06	3.64	0.65
1091	R.DPTEDDVESK.K	1134.4797	1.4693	2	2.24E-07	3.40	0.60
1096	R.DPTEDDVESK.K	1134.4797	1.4693	2	1.88E-07	3.59	0.65
1178	K.PSLQTSSAR.M	946.4952	1.1512	2	5.08E-06	2.75	0.28
1181	K.PSLQTSSAR.M	946.4952	1.1512	2	1.35E-03	2.88	0.27
1418	R.LLQQGTAPAQAK.A	1225.6899	1.8556	2	9.65E-05	3.35	0.61
1419	R.LLQQGTAPAQAK.A	1225.6899	1.8556	2	1.88E-07	3.64	0.60
1422	R.LLQQGTAPAQAK.A	1225.6899	1.8556	2	2.87E-06	3.90	0.59

1563	K.ALQQEQEIEQR.L	1371.6863	2.7907	2	4.68E-07	3.10	0.55
1892	K.LQNSASATALVSR.T	1317.7121	2.8565	2	5.32E-10	3.85	0.67
1895	K.LQNSASATALVSR.T	1317.7121	2.8565	2	5.05E-10	4.28	0.68
MTA2	**Metastasis-associated protein MTA2**				**7.51E-13**	**40.19**	
954	R.LVEGESDNR.N	1018.4800	1.7264	2	1.33E-06	2.87	0.58
1427	K.TPTQLEGATR.G	1073.5586	2.0056	2	9.83E-05	2.75	0.50
2167	K.TLLADQGEIR.V	1115.6055	1.3155	2	1.21E-05	2.78	0.57
2764	K.LNPADAPNPVVFVATK.D	1652.9006	4.3134	2	7.51E-13	3.19	0.67
2765	K.LNPADAPNPVVFVATK.D	1652.9006	4.3134	2	1.55E-09	3.72	0.71
GATAD2B	**Transcriptional repressor p66-beta**				**1.00E-30**	**40.29**	
1453	K.ENINDEPVDM*SAR.R	1505.6537	1.9932	2	1.98E-08	3.72	0.75
1455	K.ENINDEPVDM*SAR.R	1505.6537	1.9932	2	3.81E-07	4.38	0.74
1535	K.ALQQEQEIEQR.L	1371.6863	1.8118	2	3.76E-07	3.21	0.54
2036	R.VIAPNPAQLQGQR.G	1391.7754	0.5732	2	3.80E-11	2.97	0.77
2140	R.LQQQAALSPTTAPAVSSVSK.Q	1984.0709	0.5662	2	1.00E-30	4.63	0.69
2142	R.LQQQAALSPTTAPAVSSVSK.Q	1984.0709	0.5662	2	9.92E-09	5.77	0.77
MBD3	**Methyl-CpG-binding domain protein 3**				**2.27E-10**	**30.24**	
1507	R.KQEELVQQVR.K	1256.6957	0.8748	2	9.96E-04	3.32	0.38
1510	R.KQEELVQQVR.K	1256.6957	0.8748	2	2.22E-03	3.30	0.35
2157	K.GKPDLNTALPVR.Q	1280.7321	0.9470	2	6.55E-08	3.57	0.63
2159	K.GKPDLNTALPVR.Q	1280.7321	0.9470	2	4.26E-07	3.47	0.61
3909	K.LSGLNAFDIAEELVK.T	1618.8687	6.5824	2	2.27E-10	4.65	0.69
3911	K.LSGLNAFDIAEELVK.T	1618.8687	6.5824	2	2.03E-09	4.77	0.65

Table S2 List of oligonucleotide sequences used in this study.

qRT-PCR primers		
TARGET GENE	**SENSE (5'-3')**	**ANTISENSE (3-5')**
GAPDH	AAGGTGAAGGTCGGAGTCAA	AATGAAGGGGTCATTGATGG
RPL4	GCTCTGGCCAGGGTGCTTTTG	ATGGCGTATCGTTTTTGGGTTGT
PGK	ATTAGCCGAGCCAGCCAAAATAG	TCATCAAAAACCCACCAGCCTTCT
HPRT	ACCCTTTCCAAATCCTCAGC	GTTATGGCGACCCGCAG
P16INK4A	GGGTCGGGTGAGAGTGG	CGAATAGTTACGGTCGGAGG
SFRP1	GGCTTCTTCTTCTTGGGGAC	ATCTCTGTGCCAGCGAGTTT
SFRP2	TCTTGCTCTTGGTCTCCAGG	CGACATAATGGAAACGCTTTG
SFRP4	CCCGGAGGATGTTAAGTGGAT	GCTGAGATACGTTGCCAAAGTT
SFRP5	CTTTTTCTGGGCTCCAATCA	AGCAGATGTGCTCCAGTGAC
MLH1	CCACGAAGGAGTGGTTATGC	ATGACTGCAGCTTGTACCCC
HDAC1	ACCCGGAGGAAAGTCTGTTAC	GGTAGAGACCATAGTTGAGCAGC
HDAC2	GCTCTCAACTGGCGGTTCAG	AGCCCAATTAACAGCCATATCAG
HDAC3	GCAAGGCTTCACCAAGAGTC	CTGTGTAACGCGAGCAGAAC
HDAC4	GACCTGACCGCCATTTGC	GGGAGAGGATCAAGCTCGTTT
HDAC5	GGGAACCATCCTTGGAAATC	GAACTGGGCATGGCTCTTG
HDAC6	CCGGAGGGTCCTTATCGTAG	GCGGTGGATGGAGAAATAGA
HDAC7	AGCAGCTTTTTGCCTCCTGTT	TCTTGCGCAGAGGGAAGTG
HDAC8	TTTGAGCGTATTCTCTACGTGGA	ACACTGTAGTACCGTCCCTTC
HDAC9	GAGTACCTTGAAGCATTCAGGAC	CGTCACTTTGTACCCTCCTAGAG
HDAC10	GCTACCACCTGGAGTCACTG	CTCTAGGGCACTCTGACATGG
HDAC11	GCACACGAGGCGCTATCTTA	AAGGAAGTTGGGGAGGAAGA
TIMP2	AACGACATTTATGGCAACCCT	CTTCTCAGGCCCTTTGAACAT
TIMP3	ATGGTGTAGACCAGCGTGC	AGGACGCCTTCTGCAACTC
RCOR1	GATTGGGTGACCAGACCAAC	GTCGGACCCCAGTACCAG
CHD4	ATGTTCAAGTAAGCAGCCCG	CCATCCTCAATGAGCCTTTC
CHD3	GAACTCTCTCCATTTGGCCC	AAAGCCTTCAGCCAGTTCAT
SIN3A	TGCTCAGGGATGCACTACAA	GCTGAGAGGGACACGCAGT
GAPDH	AAGGTGAAGGTCGGAGTCAA	AATGAAGGGGTCATTGATGG
HDAC1 (human specific)	AGGACTGTCCAGTATTCGATGG	CTCGGACTTCTTTGCATGGTG
P53	CCGCAGTCAGATCCTAGCG	AATCATCCATTGCTTGGGACG
ChIP primers		
TARGET PROMOTER	**SENSE (5'-3')**	**ANTISENSE (3-5')**
MLH1	CCCAGCAACCCACAGAGTTGAG	CGGAAGTGCCTTCAGCCAATC
p16INK4A	GATTATAGACGTGAGCCACCGC	AGGCAGGAGAATCGCTTGAAC
SFRP1	GCACCGCAGCTAGAGAACCGA	CTGCTTCCTAATTTCAACCAACAGCCC
SFRP2	TGGCAACCCAGCAGAAACTTC	ACGCGCTTGCTGGAAGGGAATTC
SFRP4	GCCCCCTACCGGAGAAAGCAAATA	CGGATACAAGAGGGTGCGGGAGAG
TIMP2	CCCGGCTAATTTCTTGTGTTTT	GAGCGAGACTCCATCTCAAAAG
TIMP3	ACAGGATGAAGCGGAAGAGA	ATTTCCCTGAACGTCAGCAG
pLKO.1 knockdown vectors		
TARGET	**FULL HAIRPIN SEQUENDE**	
HDAC1#1	CCGGGCCGGTCATGTCCAAAGTAATCTCGAGATTACTTTGGACATG	

	ACCGGCTTTTT	
HDAC1#2	CCGGCCGCAAGAACTCTTCCAAC TTCTCGAGAAGTTGGAAGAGTTC TTGCGGTTTTT	
CHD4#1	CCGGGCTGACACAGTTATTATCT ATCTCGAGATAGATAATAACTGT GTCAGCTTTTT	
CHD4#2	CCGGGCGGGAGTTCAGTACCAAT AACTCGAGTTATTGGTACTGAAC TCCGCTTTTT	

Table S3 List of antibodies used in this study

Target protein	Application	Antibody name	Conditions used
DNMT1	ChIP	D4692 (Sigma)	5 ul
DNMT3B	ChIP	House-made	0.5ul
HDAC1	ChIP	ab7028 (Abcam)	3 ul
CHD4	ChIP	4H4 (Sigma)	5 ul
HDAC1	western/IP	5356 (Cell Signaling technologies)	1/1000
HDAC2	western/IP	2540 (Cell Signaling Technologies)	1/1000
CHD4	western/IP	4H4 (Sigma)	1/1000
MTA1	western/IP	M7693 (Sigma)	1/1000
MTA2	western/IP	M7569 (Sigma)	1/1000
RBBP4	western/IP	2566 (Epitomics)	1/1000
RBBP7	western/IP	R4279 (Sigma)	1/1000
a-tubulin	western	sc-5286 (Santa Cruz)	1/1000
GFP	western	sc-8334 (Santa Cruz)	1/5000
ß-actin	western	A2547 (Sigma)	1/5000
DNMT1	western/IP	Abcam	1/1000
DNMT1	Western/IP	D4692 (Sigma)	1/1000