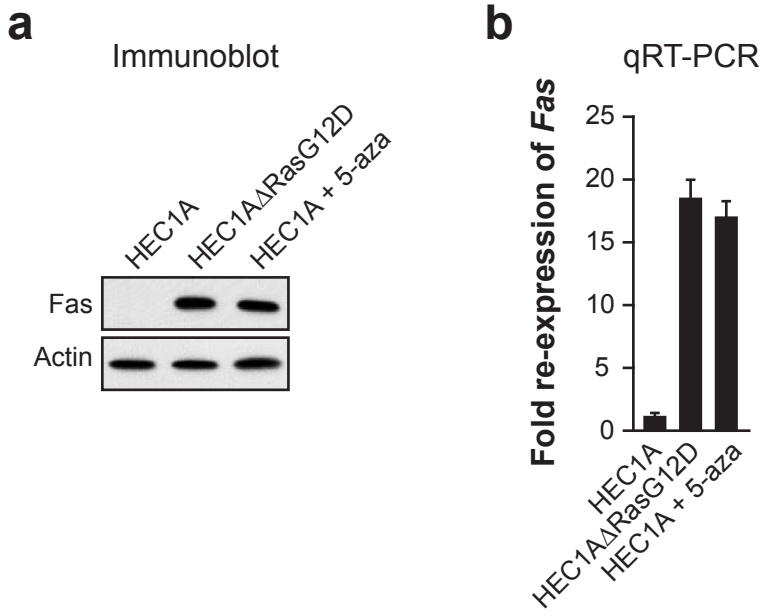
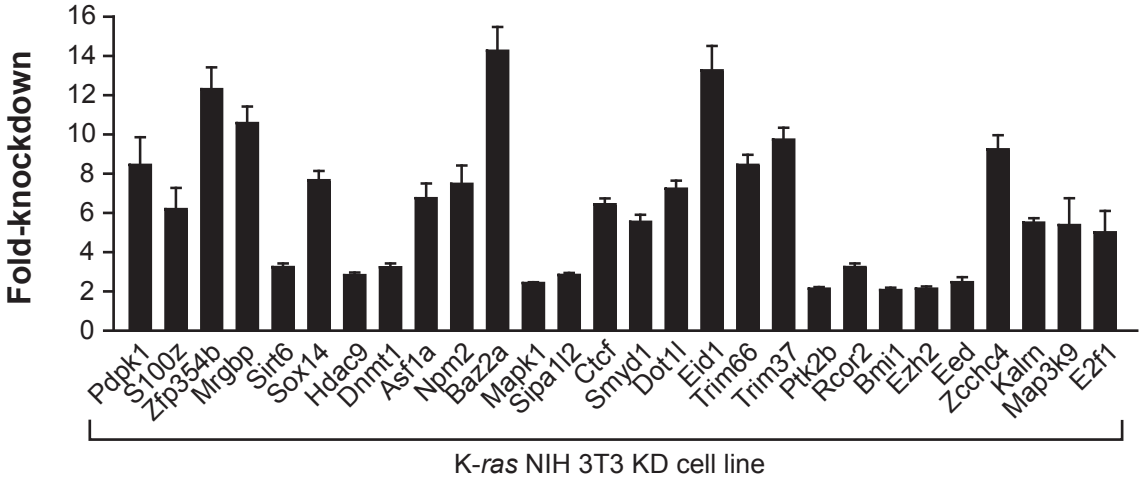
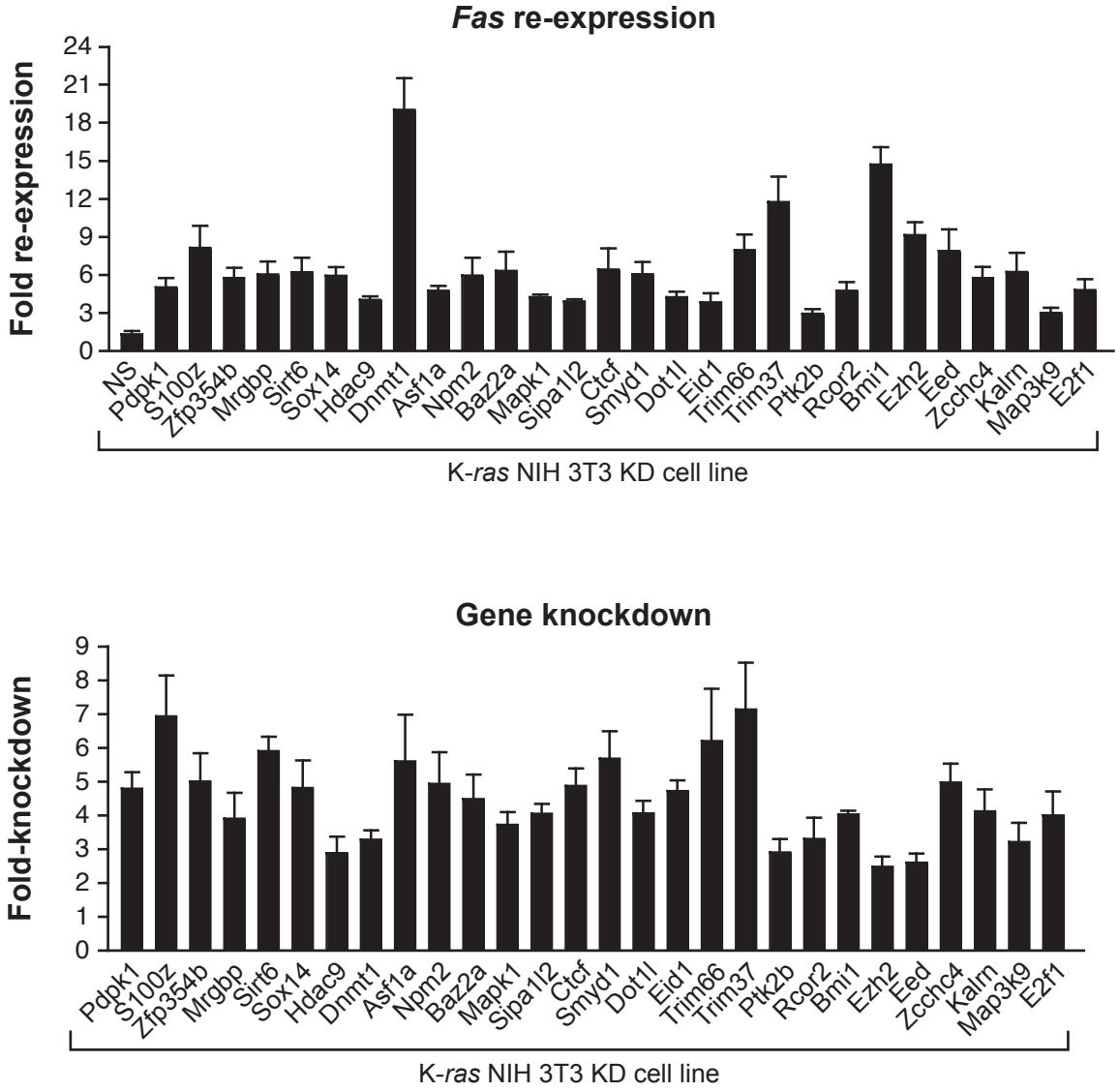


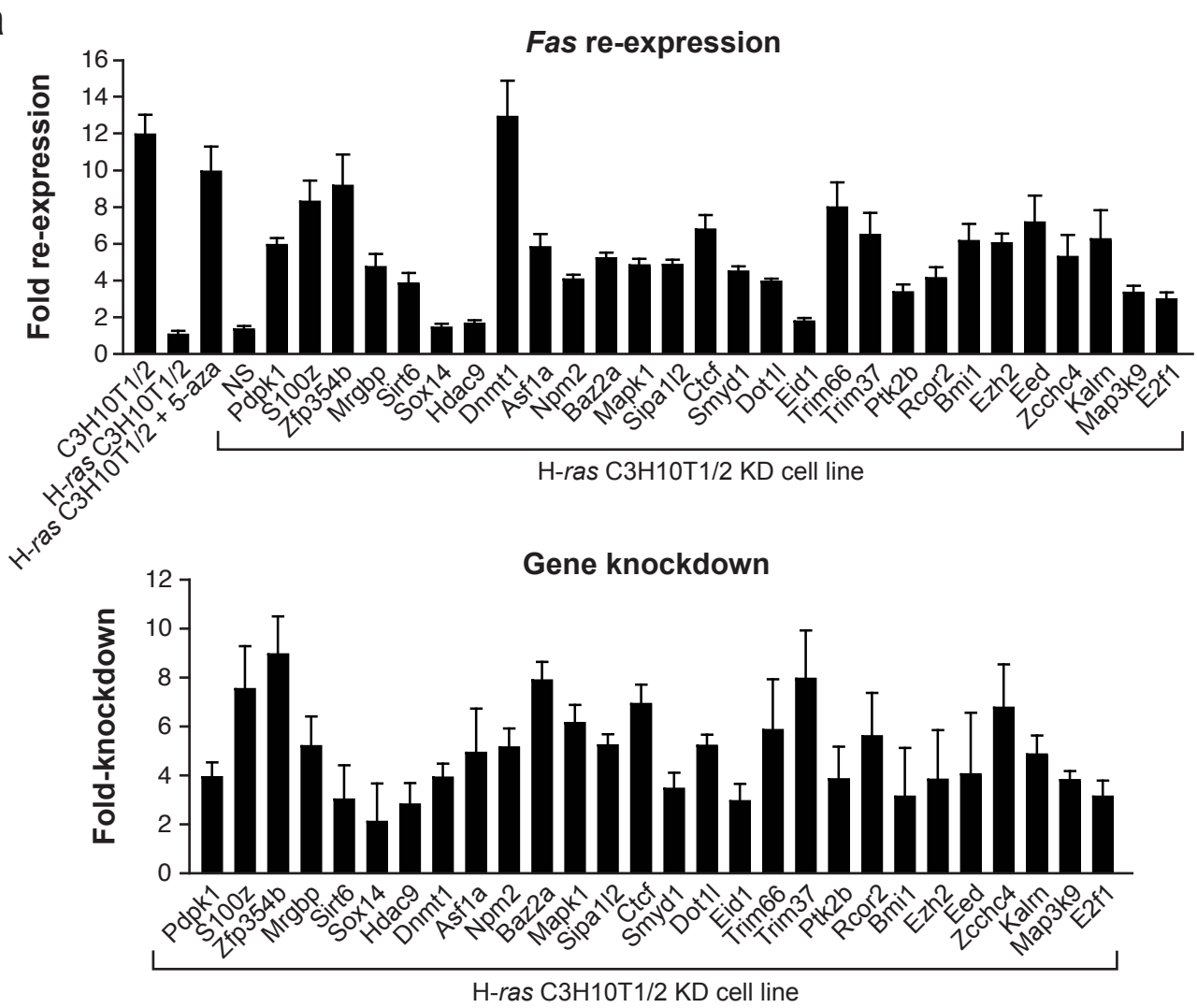
Supplementary Figure 1 Analysis of *Fas* gene expression in human endometrial cancer HEC1A cells. **a**, Immunoblot analysis. HEC1A cells contain one normal and one activated *ras* allele (RasG12D). In HEC1AΔRasG12D cells, the activated *ras* allele has been deleted[1]. Fas expression was monitored in HEC1A cells, in HEC1AΔRasG12D cells and in HEC1A cells treated with 5-aza. Actin was monitored as a loading control. **b**, Quantitative real-time RT-PCR (qRT-PCR) analysis monitoring *Fas* expression. Error bars indicate standard error.

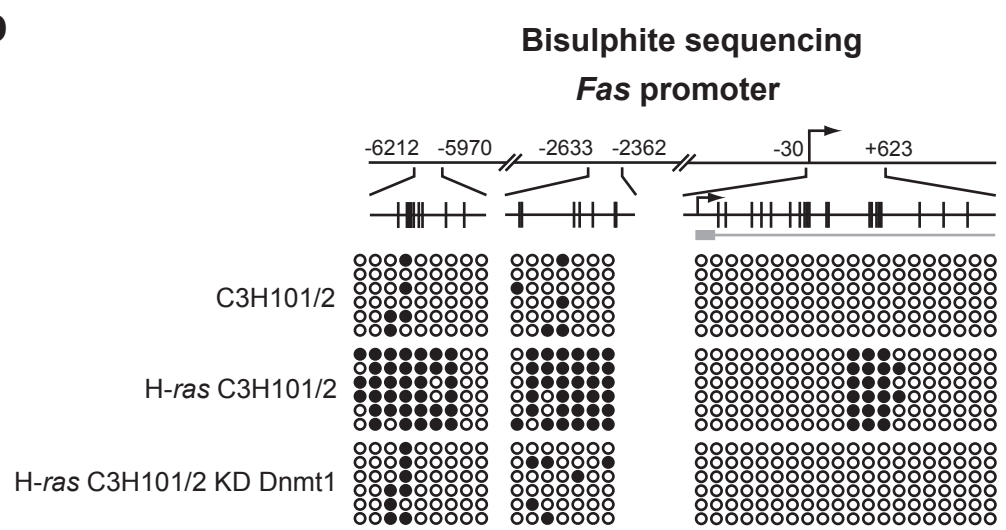


Supplementary Figure 2 Analysis of target gene expression in the K-*ras* NIH 3T3 KD cell lines. Quantitative real-time RT-PCR (qRT-PCR) was used to analyze target gene expression in each of the 28 K-*ras* NIH 3T3 KD cell lines. Error bars indicate standard error.

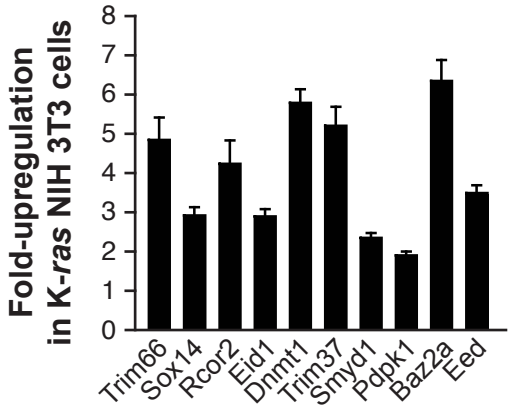


Supplementary Figure 3 Confirmation of all 28 RESEs using a second, unrelated shRNA directed against the target gene. qRT-PCR analysis shows that a second, unrelated shRNA directed against the target gene also resulted in *Fas* re-expression (top) and decreased expression of the target gene (bottom). NS, nonsilencing shRNA. Error bars indicate standard error.

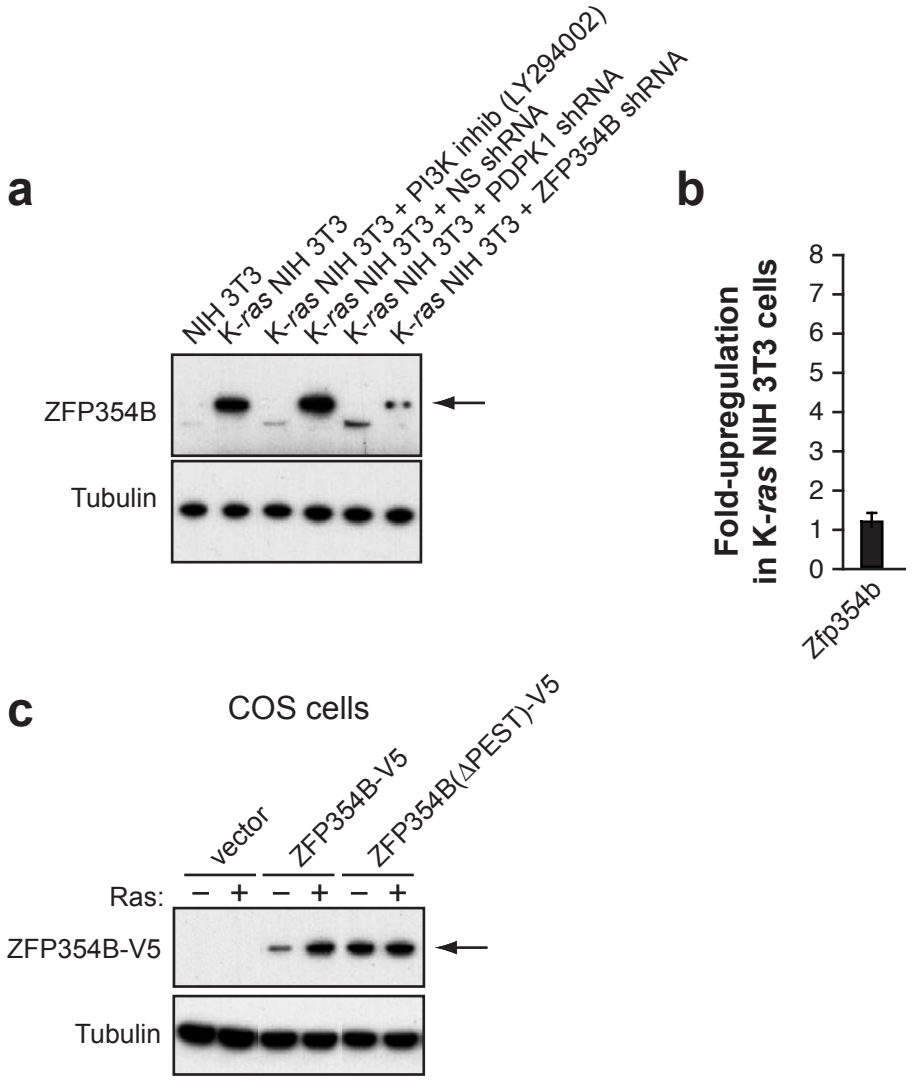




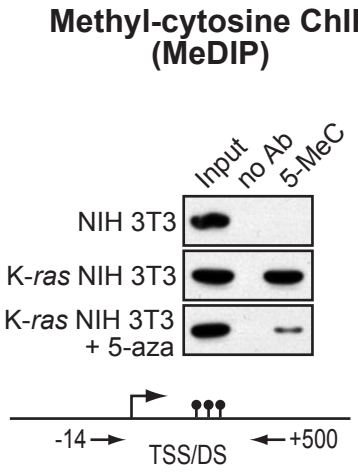
Supplementary Figure 4 Knockdown of the 28 RESEs in a second, unrelated cell line, H-*ras* transformed murine C3H10T1/2 fibroblasts, results in *Fas* re-expression. a, qRT-PCR analysis reveals that knockdown of each of the 28 RESEs resulted in *Fas* re-expression (top) and decreased expression of the target gene (bottom) in C3H10T1/2 cells. NS, nonsilencing shRNA. Error bars indicate standard error. **b,** Bisulphite sequencing analysis of *Fas*. Each circle represents a CpG dinucleotide. Open (white) circles denote unmethylated CpG sites; filled (black) circles indicate methylated CpG sites. Each row represents a single clone; for each cell line, six clones were sequenced. The regions of the promoter analyzed are shown. The position of the transcription start-site is indicated by the arrow, and positions of the CpG dinucleotides are shown to scale by vertical lines.



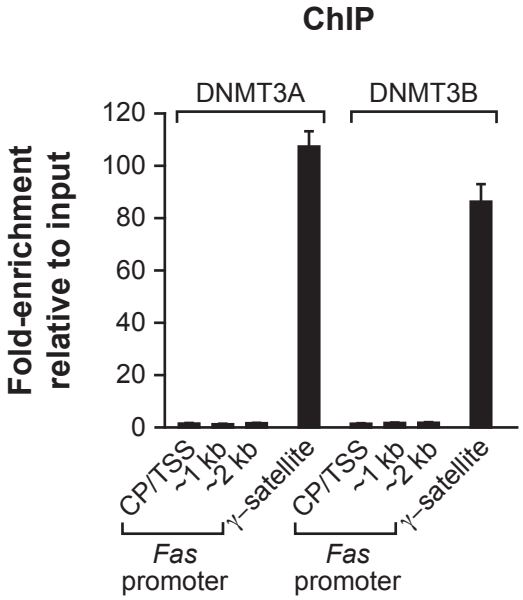
Supplementary Figure 5 Several RESEs are upregulated at the transcriptional level in K-*ras* NIH 3T3 cells. Quantitative real-time RT-PCR (qRT-PCR) was used to analyze RESE gene expression in K-*ras* NIH 3T3 cells compared to NIH 3T3 cells. Values are expressed as fold upregulation in K-*ras* NIH 3T3 cells relative to expression in NIH 3T3 cells. Error bars indicate standard error.



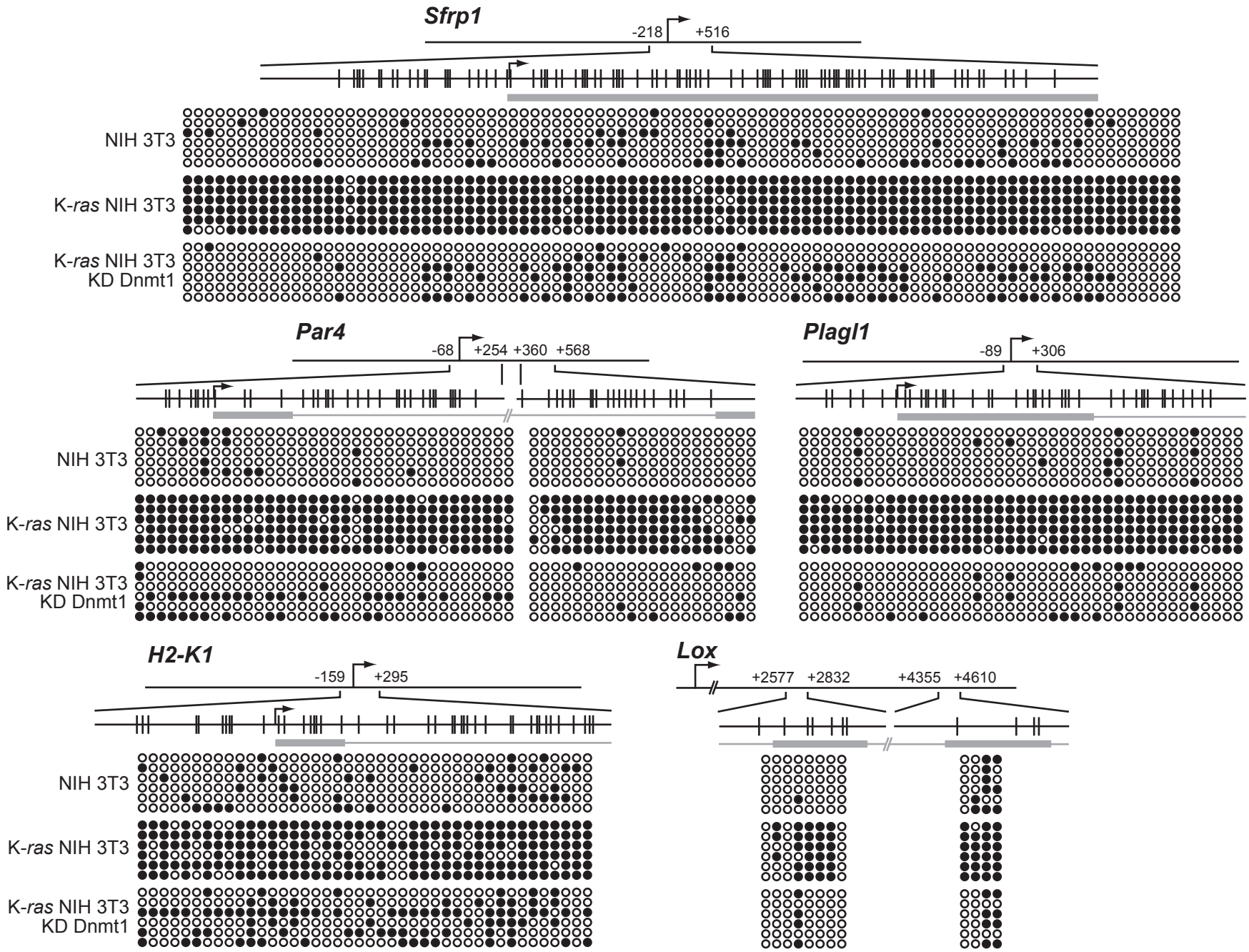
Supplementary Figure 6 ZFP354B is upregulated at the post-transcriptional level by K-Ras. **a,** Immunoblot analysis showing up-regulation of ZFP354B protein expression in K-*ras* NIH 3T3 cells compared to NIH 3T3 cells. Addition of the phosphoinositide-3 kinase (PI3K) inhibitor LY294002 prevented upregulation of ZFP354B; PI3K is a downstream effector of Ras. ZFP354B upregulation was also abrogated upon treatment with an shRNA directed against the kinase PDPK1, a RESE (see Table 1) and known downstream effector of Ras, or ZFP354B itself, but not a nonsilencing (NS) control shRNA. Endogenous ZFP354B was monitored using an anti-ZFP354B antibody, and tubulin was monitored as a loading control using an anti-tubulin antibody. **b,**Quantitative real-time RT-PCR (qRT-PCR) was used to analyze *Zfp354b* gene expression in K-*ras* NIH 3T3 cells compared to NIH 3T3 cells. The results reveal that Zfp354b is not transcriptionally upregulated in K-*ras* NIH 3T3 cells compared to NIH 3T3 cells. Error bars indicate standard error. **c,** Immunoblot analysis. Plasmids expressing activated K-Ras and/or C-terminal V5-tagged ZFP354B or a mutant derivative lacking the N-terminal PEST sequence [ZFP354B(Δ PEST)] were cotransfected into COS cells and 36 hours laters cells were harvested for immunoblot analysis. ZFP354B was monitored using an anti-V5 antibody, and tubulin was monitored as a loading control using an anti-tubulin antibody. The results show that ZFP354B protein levels increased in the presence of Ras, and that this increase depended on the presence of the PEST sequence, an element known to be involved in regulated protein stability.



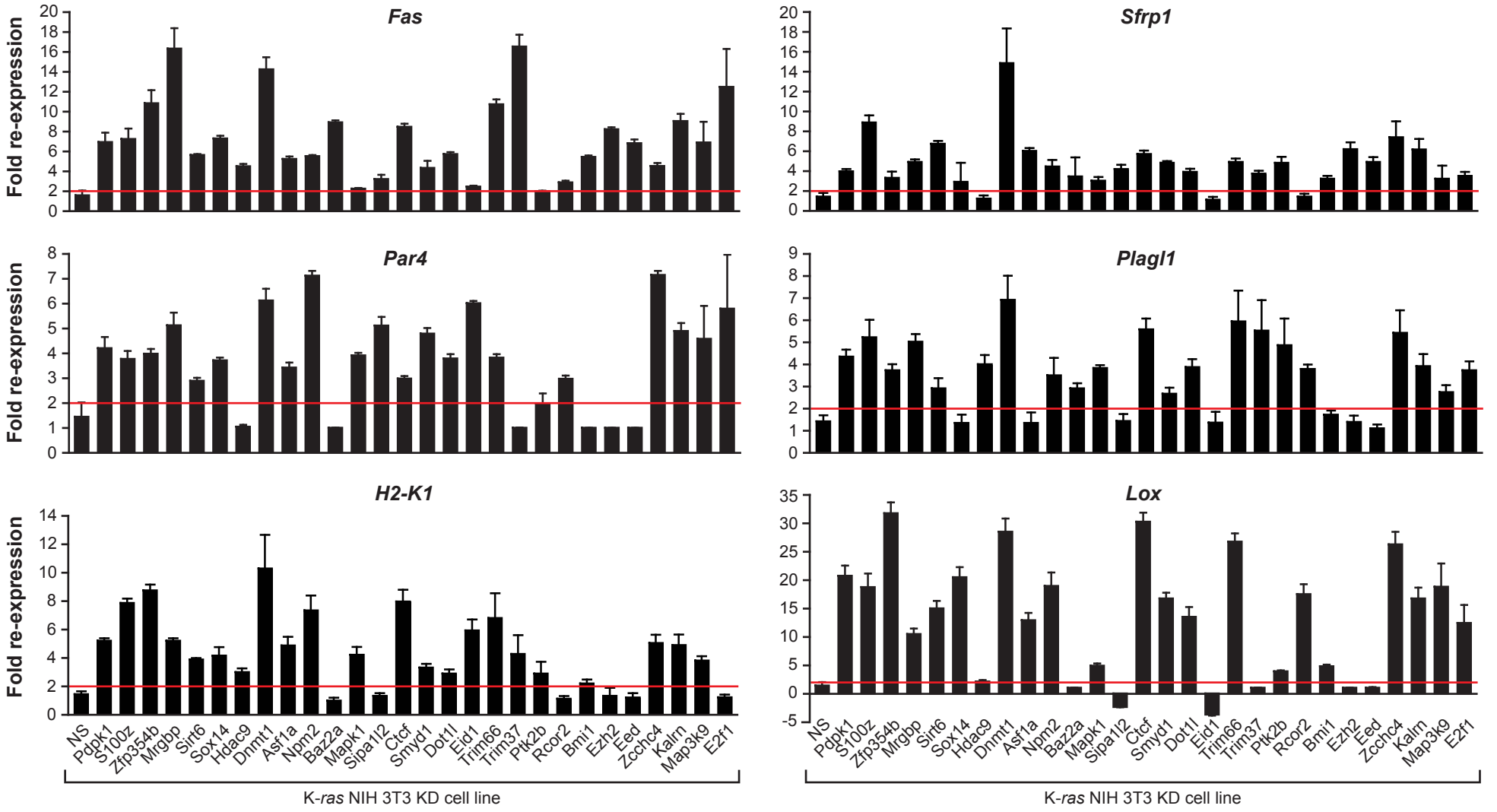
Supplementary Figure 7 Methylated DNA immunoprecipitation (MeDIP) assay of the *Fas* promoter. The primer pairs used in the analysis correspond to the transcription start-site/downstream (TSS/DS) region as shown in the schematic.



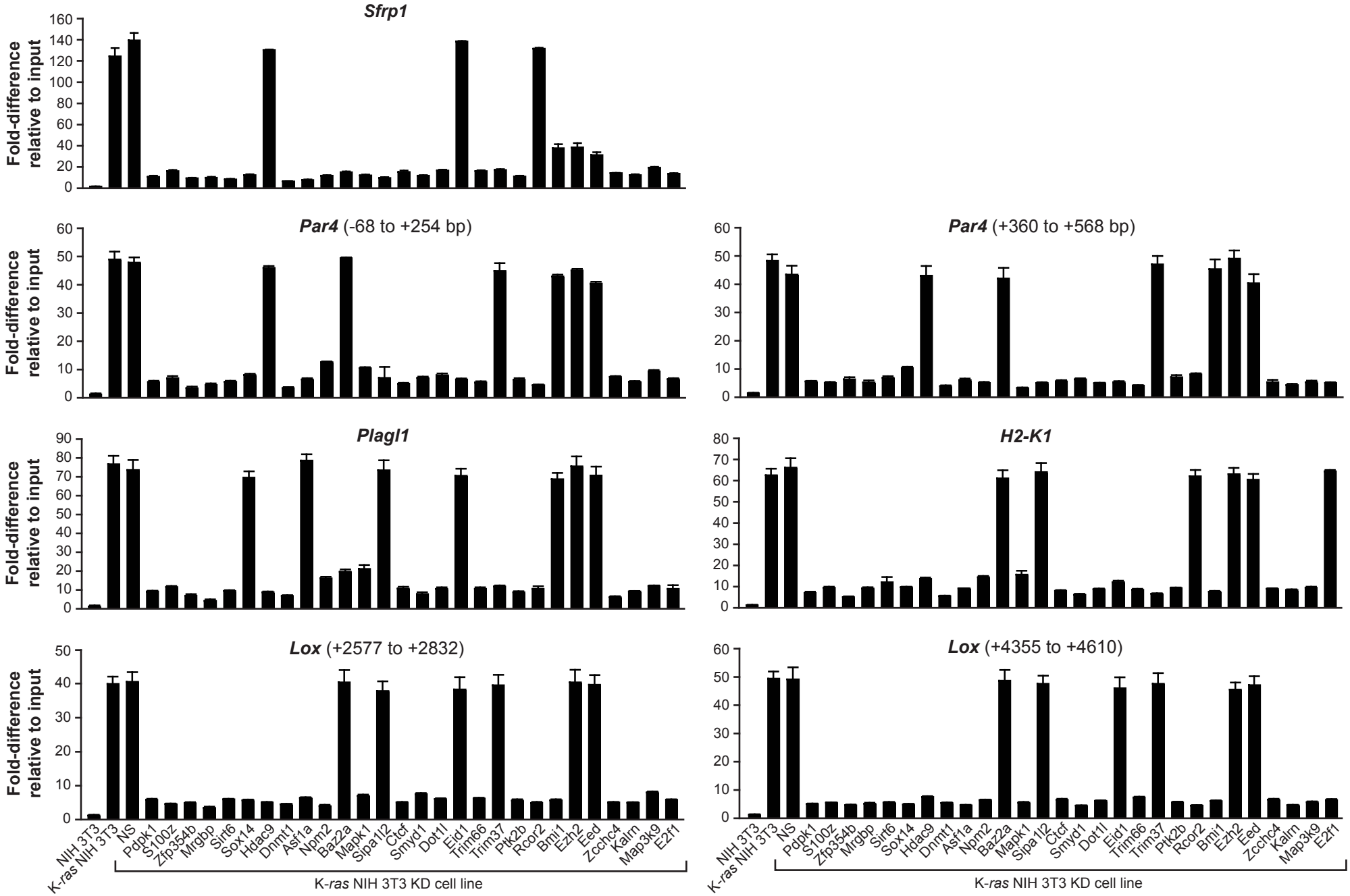
Supplementary Figure 8 DNA methyltransferases DNMT3A and DNMT3B do not detectably associate with the *Fas* promoter. Chromatin immunoprecipitation (ChIP) monitoring *Fas* promoter occupancy of DNMT3A and DNMT3B at the CP/TSS, ~1 kb upstream of the TSS, ~2 kb upstream of the TSS. As a control, binding of DNMT3A and DNMT3B was also monitored at the gamma satellite region, a known target of DNMT3A and DNMT3B[2]. Values are expressed as the fold-enrichment relative to input, and have been corrected for background. Error bars indicate standard error.



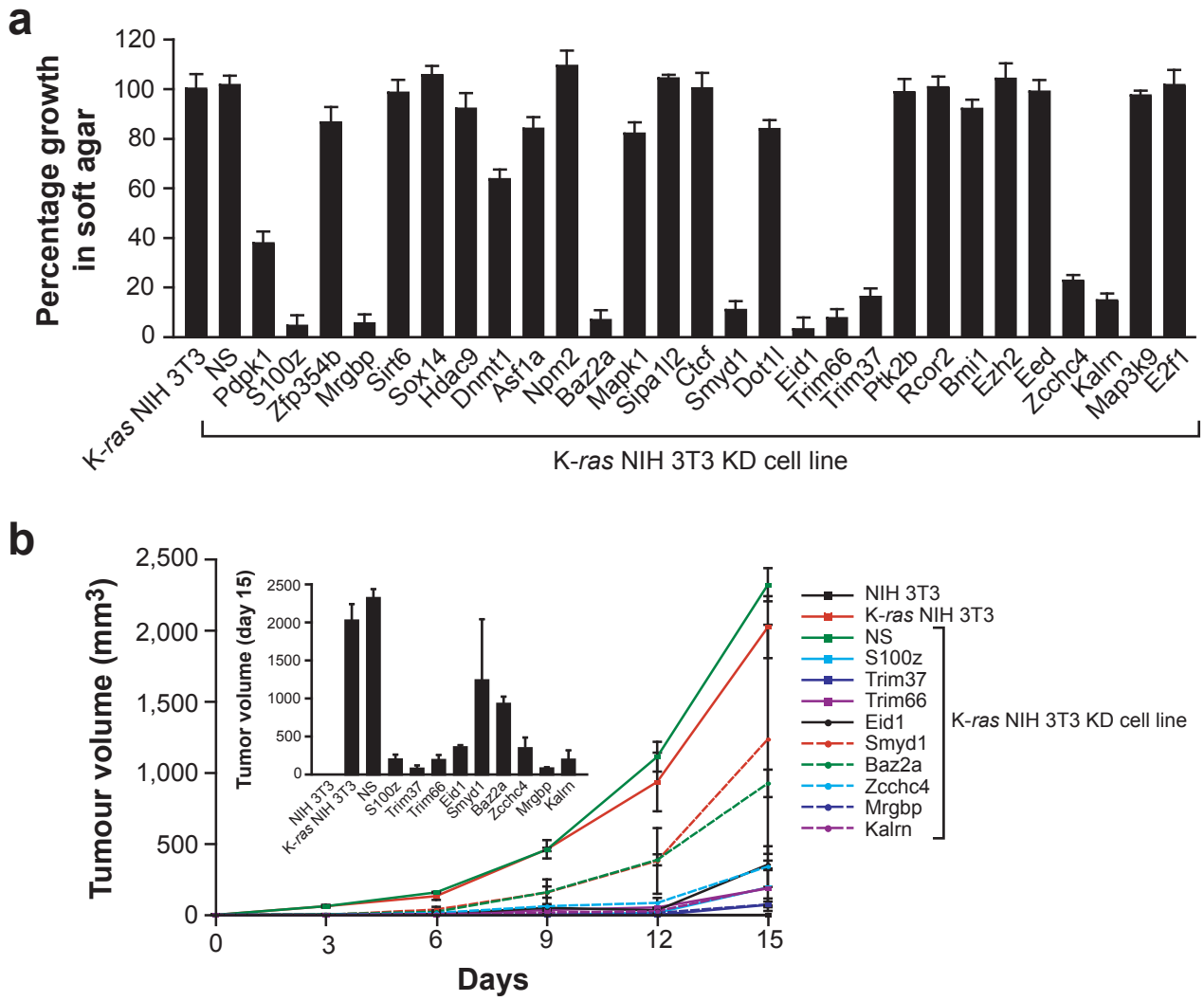
Supplementary Figure 9 Hypermethylation of *Sfrp1*, *Par4, Plagl1, H2-K1,* and *Lox* in K-*ras* NIH 3T3 cells. Bisulphite sequencing analysis. Each circle represents a CpG dinucleotide. Open (white) circles denote unmethylated CpG sites; filled (black) circles indicate methylated CpG sites. Each row represents a single clone; for each cell line, six clones were sequenced. The region(s) of the promoters analyzed is shown. The position of the transcription start-site is indicated by the arrow, and positions of the CpG dinucleotides are shown to scale by vertical lines. Exons and introns are indicated by gray thick and thin lines, respectively.



Supplementary Figure 10 Ras directs epigenetic silencing of multiple, unrelated genes through a largely common pathway. Quantitative real-time RT-PCR (qRT-PCR) analysis monitoring re-expression of *Fas*, *Sfrp1, Par4*, *Plagl1, H2-K1* and *Lox* following knockdown of each of the 28 RESEs. NS, nonsilencing shRNA. Values are expressed as fold re-expression relative to expression of the gene in K-*ras* NIH 3T3 cells. The red line indicates 2-fold re-expression. Error bars indicate standard error.



Supplementary Figure 11 MeDIP analysis of the *Sfrp1*, *Par4, Plagl1, H2-K1*, and *Lox* hypermethylated regions following knock-down of each of the 28 RESEs. MeDIP analysis following knockdown of each of the 28 RESEs. NS, nonsilencing shRNA. Values are expressed as the fold-difference relative to input, and have been corrected for background.



Supplementary Figure 12 Requirement of factors involved in Ras-mediated epigenetic silencing for a fully transformed phenotype. **a**, Soft agar growth assay. The 28 K-ras NIH 3T3 KD cell lines were tested for their ability to grow in soft agar. NS, nonsilencing shRNA. Values are expressed as percentage growth relative to parental K-ras NIH 3T3 cells. Error bars indicate standard error (n=3). **b**, Tumour formation assay. Each of the indicated K-ras NIH 3T3 KD cell lines was subcutaneously injected into the flanks of nude mice, and tumour volume was measured every 3 days for 15 days (n=3 mice per time point). Error bars indicate standard error (n=3 mice per time point).

Supplementary Table 1 | Source ID numbers and clone locations for shRNAs obtained from Open Biosystems, and sequences of synthesized shRNAs

Gene	Source ID	Clone Location
Asf1a	V2MM_64136	SM2244-F-6
	V2MM_71706	SM2238-A-2
Baz2a	V2MM_85159	SM2467-F-2
	V2MM_85157	SM2108-H-8
Bmi1	V2MM_10594	SM2169-C-12
Ctcf	V2MM_190309	SM2165-B-1
	V2MM_192417	SM2165-D-3
Dnmt1	V2MM_46797	SM2437-D-12
Dot1l	V2MM_193454	SM2256-A-8
Eed	V2MM_73225	SM2174-G-7
	V2MM_65179	SM2009-A-7
Eid1	V2MM_61927	SM2214-G-10
	V2MM_70375	SM2020-A-12
Ezh2	V2MM_30422	SM2432-E-11
	V2MM_35988	SM2396-F-7
E2f1	V2MM_28115	SM2433-F-2
	V2MM_32206	SM2167-C-12
Hdac9	V2MM_159316	SM2202-A-4
Kalrn	V2MM_160069	SM2130-E-7
	V2MM_84498	SM2144-F-10
Mapk1	V2MM_132158	SM2106-G-2
	V2MM_34173	SM2396-E-11
Map3k9	V2MM_70200	SM2012-G-9
	V2MM_63859	SM2011-A-5
Mrgbp	V2MM_202249	SM2487-E-6
	V2MM_105745	SM2162-H-1
Npm2	V2MM_93385	SM2265-E-1
	V2MM_93381	SM2471-D-1
Pdpk1	V2MM_78532	SM2021-G-9
	V2MM_75859	SM2004-F-9
Ptk2b	V2MM_26156	SM2434-B-11
	V2MM_21947	SM2187-E-10
Rcor2	V2MM_2246	SM2385-A-12
	V2MM_7624	SM2604-D-5
Sipa1l2	V2MM_130034	SM2106-D-2
	V2MM_130033	SM2358-E-1
Sirt6	V2MM_93633	SM2139-G-10
	V2MM_93636	SM2451-H-4
Smyd1	V2MM_74820	SM2167-E-4
	V2MM_74911	SM2181-A-12
Sox14	V2MM_193113	SM2507-D-4
	V2MM_193113	SM2298-G-2
S100z	V2MM_150368	SM2059-C-3
	V2MM_150367	SM2032-G-11

Trim37	V2MM_95365	SM2143-F-9
	V2MM_226566	SM2464-A-3
Trim66	V2MM_193395	SM2269-B-4
	V2MM_93826	SM2255-H-9
Zcchc4	V2MM_107407	SM2612-F-6
	V2MM_202115	SM2496-B-8
Zfp354b	V2MM_70272	SM2007-F-3
	V2MM_70504	SM2026-C-5

Gene	Sequence (5' → 3')
Bmi1	TGCTGTTGACAGTGAGCGCGCAGATGAGGAGAAGAGGATTTAGTGAAGCCACAGATGTA AATCCTCTTCTCCTCATCTGCATGCCTACTGCCTCGGA
Dnmt1	TGCTGTTGACAGTGAGCGCGCCCATCCTCAGGGACCATATTAGTGAAGCCACAGATGTA ATATGGTCCCTGAGGATGGGCTTGCCTACTGCCTCGGA
Dot1l	TGCTGTTGACAGTGAGCGCGGAGCGATTCGCAAACATGAATAGTGAAGCCACAGATGTA TTCATGTTTGCGAATCGCTCCTTGCCTACTGCCTCGGA
Hdac9	TGCTGTTGACAGTGAGCGCGGACATTTAATTCTGAGATTATAGTGAAGCCACAGATGTA TAATCTCAGAATTAAATGTCCTTGCCTACTGCCTCGGA

Supplementary Table 2 | Primer sequences for bisulphite sequencing, methylated DNA immunoprecipitation, chromatin immunoprecipitation and quantitative real-time RT-PCR analyses

Bisulphite sequencing

Gene	Position (relative to TSS)	Primer name	Forward or reverse primer	Sequence (5' → 3')
Fas	-30/+260	FASU2	forward	GTTGTAGATATGTTGTGGATTTGGGTTG
		FASR3D2	reverse	CTAAACAAATCTATAAACCAAAATCCCTCTC
		FASR3U1 (nested)	forward	GGGTTGTTTTGTTTTTGGTAAGTTTTG
		FASR3D1 (nested)	reverse	CCAAAATCCCTCTCCAACCATACT
	+260/+623	FASR4U2	forward	GGAGAGGGATTTTGGTTTATAGATTTG
		FASR4D2	reverse	CCATCCACAATTTAACAACTCAATTCC
		FASR4D1 (nested)	forward	AAATATCCACCAATTCAACCATCCAC
		FASR4U1 (nested)	reverse	GTATGGTTGGAGAGGGATTTTGGT
	-2633/-2362	FAS2.6U	forward	GAAAAGAAGTAGAAATAGAAGTTGAG
		FAS2.6D	reverse	CTACATCCCAACTATAACTTTACTAC
	-6212/-5970	FAS6.2U	forward	GTTTGGTTTATAGTTATAGAGTAGAG
		FAS6.2D	reverse	CACTAAAAAACATCATTACTTACACTAACC
H2-K1	-150/+295	H2K1U1	forward	GTGAGGTTAGGGGTGGGGGAAGTTTA
		H2K1D1	reverse	CTCTTAACTCTCTATATCTACTCCTC
		H2K1U2 (nested)	forward	GTTTTATTTTTGTTTTTAATTTGGGTTAGG
		H2K1D2 (nested)	reverse	AAATACCTCAACAAATATAAACCTAAAAA
Lox	+2577/+2632	LOXe3U1	forward	AGGGAGGGGGTTGTTAGGATTTTG
		LOXe3U2 (nested)	forward	GTTGTTAGGATTTTGTGATGGTGAGTTG
		LOXe3D1	reverse	TAACAACCACCCTCTCTCCTTTCACTC
		LOXe3D2 (nested)	reverse	CACCCCAAATAAAAAACCCATTCACTTAC
	+4355/+4610	LOXe4U1	forward	GGAAGTTATTTAGTATTTTTATTGTTTTGTTTATGTG
		LOXe4U2 (nested)	forward	GTTGTTTTTTTGTTGTGTGGGATATTAGATA
		LOXe4D1	reverse	CAACAACTAACTTACTATCACTTTCCTA
		LOXe4D2 (nested)	reverse	TCCAAATATCAAAAAACCTACCTACCTA
Par4	+360/+568	R4F	forward	TTAGGAAAGGTAAGGGGTAGAT
		R4D	reverse	CAATCATTTACTCCAAATAAAACTCCATC
	-68/+254	PARTSU	forward	AGTTAGGGATTGTTTTTAGTTTAGG
		PARTSD	reverse	CACAACTCCCCRAAACTCCCATTC
Plagl1	-89/+306	PLAGLU	forward	ATTTGTTATTTAGTTTGGGTTGGGAT
		PLAGLD	reverse	CTACATCTCTAACTACAACTAAAACAC
Sfrp1	-218+516	SFRPU1	forward	GAAAGTATTTGTTTAGTTTTTGGTTTTG
		SFRPD1	reverse	CAAATTAAACAACACCATTCTTATAACC
		SFRPU2 (nested)	forward	GTTTTGTTTTTTAAGGGGTGTTGAT
		SFRPD2 (nested)	reverse	TTATAACACAACCTCAAATCCAC

Methylated DNA immunoprecipitation (MeDIP)

Gene	Position relative to TSS	Forward or reverse primer	Sequence (5' → 3')
Fas	-14 bp	forward	CAGCCCAGAGTAACTCACTTC
	+500 bp	reverse	CATACCCACAGGCAGTCTAGA
	-2.6 kb	forward	GAAGTAGAAACAGAAGCTGAG
	-2.3 kb	reverse	TTGCTACATCCCAACTGTAAC
	-6.2 kb	forward	GGTCTACAGCCACAGAGCAGA
	-5.9 kb	reverse	TCTTCTGTCACTAGAGGGCATC
H2-K1	-50 bp	forward	GCCACTGGTTATAAAGTCCA
	+125 bp	reverse	AAAGCTGTTTCCCTCCCGAC
Lox	+2.6 kb	forward	GCTGCTAGGACCTTGTGATGG
	+2.8 kb	reverse	CACCCCAGATGAGAGGCCCA
	+4.4 kb	forward	GCTGTTTCTTTGTTGTGTGGG
	+4.6 kb	reverse	TCCAGATGTCAGGGGACCTGC
Par4	-47 bp	forward	CAGGCCGGCGAGTTTGCCGG
	+90 bp	reverse	TGCGGGTGGCCCGGAAGAGC
	+365 bp	forward	GATCGAGAAGAGGAAGCTGC
	+570 bp	reverse	TCTGGGTCGGGGTAACTTCC
Plagl1	-36 bp	forward	CGCCCCGAGCCTTGATTTAG
	+184 bp	reverse	ACTCAGGCGTCGCCGTCAGA
Sfrp1	-68 bp	forward	CTGATTGGCTGCGCGCGGGG
	+182 bp	reverse	GCAGTGCCGGGCCCCGTCCG

Chromatin immunoprecipitation (ChIP)

Fas promoter

Region	Forward or reverse primer	Sequence (5' → 3')	Position relative to TSS
CP/TSS	forward	GCCGCCTGTGCAGTGGTGA	-234
	reverse	CTGTGTGTGGGCAGCCTGCGGC	+20
~ 1kb	forward	GGCTATAGATCACCTTCATGTA	- 967
	reverse	GCAGTTAACTCAGGGACCAAG	- 722
~ 2kb	forward	GCGTTGCCATAGCATGAACT	- 2330
	reverse	GAGTTAGGGGACCATAGTCA	- 2053

Gamma satellite DNA

Forward or reverse primer	Sequence (5' → 3')
forward	TATGGCGAGGAAAACTGAAA
reverse	TTCACGTCCTAAAGTGTGTAT

Quantitive real-time RT-PCR (qRT-PCR)

Gene	Forward or reverse primer	Sequence (5' → 3')
Asf1a	forward	GGCAAAGGTTCAGGTGAACAAT
	reverse	GGATGAGTCCTGCATTCGGAG
Baz2a	forward	CACTCCTCTAGCACCTCACAC
	reverse	GGTGATGGAGGTGTGAGGTG
Bmi1	forward	TCGGCCAACTTGCAAAAGAA
	reverse	GGGACTGGCAAACAGGAAG
Ctcf	forward	CACGGGGGAGAAGCCTTATG
	reverse	CGGGTGAATGTTTTCCCACA
Dnmt1	forward	GAACCATCACCGTGCGAGAC
	reverse	CCAGTGGGCTCATGTCCTTG
Dot1l	forward	CCACCCCATACCAGGACCAT
	reverse	CTGCTGGGCTCATCCTCAGA
Eed	forward	CGAGAGGGGAAGTGTCGACTG
	reverse	GCCTCCCTCCAGGTTCTTGC
Eid1	forward	ACCTTGGTCGAGTCGCTTCC
	reverse	AACTCGTCGCCTTCCAGGTC
Ezh2	forward	GTAGCATTCAGCGGGGCTCT
	reverse	GGGTTGCATCCACCACAAAA
E2f1	forward	GGCTGGATCTGGAGACTGACC
	reverse	CTGCACCTTCAGCACCTCAG
Fas	forward	GATGCACACTCTGCGATGAAG
	reverse	CAGTGTTCACAGCCAGGAGAAT
Hdac9	forward	GCAGTCCAGGGAGCTAGACG
	reverse	GAGCTGATCATACTGTGCTAAG
H2-K1	forward	GAGCAGTGGTTCCGAGTGA
	reverse	GGTCTTCGTTCAGGGCGATG
Kalrn	forward	CCTGGACCTGTTGCTGATGG
	reverse	CTGGAGCACAGCTGCAGTCA
Lox	forward	CTCATCTGCCTGAAAGCACAC
	reverse	GGGCAAAGAGGTACATCGAAG
Mapk1	forward	ACAGAGTCCTCCCCGTCTGC
	reverse	GCATGTTTGGGTGCCATCAT
Map3k9	forward	AAGAGGATTCCCCCGGACAT
	reverse	ACACATCGCTGCCTTTGGAA
Mrgbp	forward	ACAAGCCTGTCGGGGTGAAT
	reverse	ACTGTGGGGGTCCACATCCT
Npm2	forward	GGAGCCCTGAAGCCATATTGAG
	reverse	GGCCTCTAAAGGTGCAAGTCT
Par4	forward	CCCCGAACAGACAGAAGTGGT
	reverse	CTTGCATCAGCCTCACAAGTC
Pdpk1	forward	GCAACTACGACAATCTCCTG
	reverse	CCTTTCGCTTATCCACTGGA
Plagl1	forward	GCAGCCACAGTTTCAGTTGC
	reverse	CTCTGGCTCTGGCTCAGGAT
Ptk2b	forward	TCCAGCAGACCTTCCAGCAG
	reverse	CCTTTAGGGCCGATGACCAG
Rcor2	forward	TGGGGCTATTGCAGAGGTGA
	reverse	CTGCTCAGCCTCCCATTCCT

Sfrp1	forward	CATCCATGGGGCTACAGTGA
	reverse	TGGCATGGTGAGTTTTCAGG
Sipa1l2	forward	CTCGTCGTGGCCTCAGAGAA
	reverse	TGTGACGGCCTTGGATCACT
Sirt6	forward	CTTCCCCAGGGACAAACTGG
	reverse	CGGATCTGCAGCGATGTACC
Smyd1	forward	TGGAGAAGCAGGAGCCAGTG
	reverse	TTGGTAAGCCCTGCCCTCAT
Sox14	forward	GGTGAAGAGGGAGCGAAGGA
	reverse	CTGTGGGCACCAGAGATTGG
S100z	forward	GCTGGAGATGGCTATGGACAC
	reverse	GCAACCGTCAGAGCTGCCAC
Trim37	forward	GGAGAAATTGCGGGATGCTC
	reverse	GCCCAACGACAGTTCACCAG
Trim66	forward	TTTCGTCTGGCCAACAGCAT
	reverse	CTGAAGGATGGGGAGGGATG
Zcchc4	forward	AGCTTGGAAGGCCCAGTCAG
	reverse	GCCTTGGTGCTCCAACACAC
Zfp354b	forward	GGATGAGTGGAAGAAGCTGG
	reverse	CTCCTTGTTGCAACACGGAG

SUPPLEMENTARY METHODS

Cell lines and culture conditions. Human HEC1A and HEC1AΔ*ras* derivative cells (a gift from T. A. Waldman, Georgetown University, USA) were maintained in McCoy's medium supplemented with 10% fetal calf serum (FCS) at 37°C and 5% CO_2. Murine C3H10T1/2 cells stably transfected with activated human Ha-*ras* (C3H10T1/2-Ras) and their control counterparts (C3H10T1/2-Neo) (a gift from E. J. Taparowsky, Purdue University, USA) and COS-M6 cells (generously provide by M. Koken, CNRS, France) were maintained in Dulbecco's modified Eagle's medium (DMEM) supplemented with 10% FCS. For 5-aza-2'-deoxycytidine (5-aza) treatment, cells were treated with 10 μM 5-aza for 72 h.

Plasmids. The human ZFP354B open reading frame (accession number BC112111.1) was cloned into the vector PEF6V5b (source) in frame with the C-terminal V5 tag. The PEST sequence deletion derivative (ΔPEST), in which amino acids 80-102 were deleted, was derived by PCR using the wild-type expression vector as the substrate, Pfu DNA polymerase (Stratagene) and the following primers: ZD1 (forward), 5'-GAGAAA GATGCCGGCGGATTTCAGGAGCAGATAAGGAAAAGATTG-3' and ZD2 (reverse), 5'-CTCCTGAAATCCGCCGGCATCTTTCTCCACCTCCCAGGGATC-3'. The plasmids pBABE-puro and pBABE-puro-KRASV12 were obtained from Addgene.

Immunoblot analysis. Extract preparation and immunoblot analysis were performed essentially as described in the Methods section accompanying the main text. The PI3K inhibitor LY294002 (LC Laboratories) was added at a concentration of 25 μM for 24 h. Transient cotransfections in COS-M6 cells were performed using Effectene (Qiagen) and, after 24 h, cells were serum-starved for 12 h prior to extract preparation. Antibodies were obtained as follows: anti-ZFP354B antibody (raised against a synthetic peptide corresponding to amino acids 126-143 of the murine protein, and affinity

purified on a peptide coupled to agarose), anti-Actin (A-5106; Sigma) and anti-Tubulin (T-5368; Sigma).

Quantitative real time RT-PCR. Total RNA was isolated using TRIZOL (Invitrogen) 7 days following retroviral transduction and puromycin selection. Reverse transcription was performed using SuperScript II Reverse Transcriptase (Invitrogen) as per the manufacturer's instructions, followed by quantitative real-time PCR as described above. The sequences of the primers used for quantitative real-time PCR are provided in Supplemental Table 2.

Chromatin immunoprecipitation (ChIP). ChIP assays were performed as described in the Methods section accompanying the main paper, using antibodies anti-DNMT3A (IMG-268A; Imgenex) and anti-DNMT3B (Ab2851; Abcam). The sequences of the primers used for amplifying the ChIP products are provided in Supplementary Table 2. ChIP products were visualized by autoradiography, or analyzed by quantitative real-time PCR using Platinum SYBR Green qPCR SuperMix-UDG with Rox (Invitrogen). Calculation of fold-differences was done as previously described[3].

Supplementary References

1. Kim, J. S., Lee, C., Foxworth, A. & Waldman, T. B-Raf is dispensable for K-Ras-mediated oncogenesis in human cancer cells. *Cancer Res.* **64**, 1932-1937 (2004).

2. Bachman, K. E., Rountree, M. R. & Baylin, S. B. Dnmt3a and Dnmt3b are transcriptional repressors that exhibit unique localization properties to heterochromatin. *J. Biol. Chem.* **276**, 32282-32287 (2001).

3. Pfaffl, M. W. A new mathematical model for relative quantification in real-time RT-PCR. *Nucleic Acids Res.* **29**, e45 (2001).