Supplementary Results

Time-course evaluation of TALE-TET1-indcued effects on *HBB* promoter methylation and gene expression

To test whether the -266 CpG demethylation and increased *HBB* gene expression induced by HB-4, HB-5-, and HB-6 are stable over time, we assayed these parameters in a more extended time-course experiment. K562 cells transfected with expression plasmids encoding HB-4, HB-5, HB-6, or a control TALE-TET1 fusion targeted to the *KLF4* locus were assayed for -266 CpG demethylation and *HBB* gene expression at 4, 7, 14, and 30 days post-transfection. HB-4, HB-5, and HB-6 fusions all showed their highest levels of fold-activation at post-transfection day 4 with *HBB* expression steadily decreasing by day 30 to the same level observed with the control *KLF4*-targeted TALE-TET1 protein (**Supplementary Fig. 10a**). Strikingly, for all three *HBB*-targeted TALE-TET1 proteins, the extent of -266 CpG methylation over time in the population of transfected cells directly paralleled the fold-activation of *HBB* gene expression while the methylation status of another CpG at position -306 did not change significantly during the course of the experiment (**Supplementary Fig. 10b**).

Construction and Testing of Engineered ZF-TET1 Fusion Proteins Targeted to the Human KLF4 and HBB Genes

To test the feasibility of targeting TET1 activity using engineered zinc finger (ZF) proteins, we constructed ZF arrays targeted to two sites in the *KLF4* gene and to six sites in the *HBB* gene. These zinc finger arrays each consisted of six fingers and were assembled using two-finger units according to the method originally described by Moore et al.[1], and similar to the ZF engineering approach previously used by Sangamo Biosciences[2]. Of the two ZF-TET1 fusions targeted to *KLF4*, one failed to demethylate nearby CpGs while the other was able to induce demethylation of CpGs located 6 and 24bp downstream of the ZF binding site by 61% and 18%,

respectively (**Supplementary Fig. 8**). One ZF-TET1 fusion targeted to the -266 CpG in the *HBB* promoter failed to induce demethylation but all five fusions targeted to the region approximately 100 bp downstream of the transcription start site were able to demethylate target CpGs with efficiencies comparable to those observed with TALE-TET1 proteins (**Supplementary Fig. 9**).

Supplementary Methods

ZF-TET1 Fusion Protein Design and Construction

Six-finger zinc finger arrays were assembled using two-finger units derived from three-finger proteins selected by the OPEN method[3]. Assembled six-finger proteins were fused to the catalytic domain of TET1 using the linker sequence Leu-Arg-Gly-Ser and to an N-terminal nuclear localization signal with expression of the ZF-TET1 fusion protein driven by an EF1alpha promoter.

Western Blotting

Transfected cells were lysed in radioimmunoprecipitation assay protein extraction buffer (Cell Signaling) and centrifuged for 5 min at 4°C to harvest the supernatant. The concentration of the extracted protein was determined using a Thermo Scientific protein assay kit. Ten micrograms of the extracted protein were loaded per lane onto 4% to 12% Tris-glycine gels (Life Technologies) for electrophoresis, and electro-transferred to nitrocellulose membrane (Life Technologies). This membrane was blocked with 5% nonfat dry milk in Tris-buffered Saline-Tween buffer [25 mM Tris (pH 7.4), 137 mM NaCl, 2.7 mM KCl, 0.1% Tween 20] for 1 hour at room temperature, followed by incubation with monoclonal Anti-FLAG M2 antibody (Sigma, F3165, 1:7,500 diltution) and β-actin (C4) HRP monoclonal antibody (Santa Cruz Biotechnology, sc-47778, 1:40,000 dilution) in blocking buffer for 2 hours at room temperature. After washing with TBS-T buffer, the membrane was incubated with goat anti-mouse IgG (H+L) - HRP conjugate antibody (Bio-Rad Laboratories, 172-1011, 1:10,000 dilution) in blocking buffer for 1 hour at room temperature. The membrane was developed using ImmunoCruz chemiluminescence system (Santa Cruz Biotechnology) and exposed to BioMax XAR film (Kodak).

Additional Experimental Details for Bisulfite PCR

All PCR Primer sequences are provided in **Supplemental Table 1**

Standard Illumina multiplex adapters and indexes were added by PCR for both *KLF4* amplicons and for and *HBB* amplicon #3 as described below.

KLF4 PCR Conditions #1 (For KL1 TALE-TET1 and for ZF-TET1 samples)

Initial amplification and addition of Illumina multiplex adapters was performed on 1 µl of bisulfite-converted genomic DNA in a 40 µl reaction using Kapa HiFi HotStart Uracil+ ReadyMix, a final concentration of 6 nM for each initial primer and 30 nM for each primer containing Illumina adapter and the following PCR conditions: 95°C for 5 minutes; 10 cycles of 98°C for 20 seconds, 68.5°C for 15 seconds, 72°C for 20 seconds; 32 cycles of 98°C for 20 seconds, 72°C for 25 seconds; 72°C for 5 minutes. PCR amplicons were purified with Agencourt AMpure XP PCR purification beads (Beckman Coulter). Approximately 2 ng of purified initial PCR was used as template for PCR with Illumina Multiplexing PCR primer 1.0 and one of 60 Illumina Index primers (**Supplementary Table 1**) using 2X Phusion Hot Start Flex DNA polymerase (NEB) and the following PCR conditions: 98°C for 2 minutes; 10 cycles of 98°C for 20 seconds, 57°C for 30 seconds, 72°C for 30 seconds; 72°C for 5 minutes. PCR was purified with Agencourt AMpure XP PCR purification beads (Beckman Coulter), quantified on a QIAxcel (Qiagen) and equal molar amounts of each amplicon were combined for high-throughput sequencing.

KLF4 PCR Conditions #2 (For KL2 TALE-TET1 samples)

Exactly as described for KLF4 PCR conditions #1 above with the exception that the initial PCR contained 1% DMSO and used the following conditions: 95°C for 5 minutes; 10 cycles of 98°C

for 20 seconds, 66°C for 15 seconds, 72°C for 20 seconds; 32 cycles of 98°C for 20 seconds, 72°C for 25 seconds; 72°C for 5 minutes.

HBB PCR Conditions #3 (for -307/-266 CpGs)

Exactly as described for KLF4 PCR conditions #1 above but with the following PCR conditions for initial PCR: 95°C for 5 minutes; 10 cycles of 98°C for 20 seconds, 63.2°C for 15 seconds, 72°C for 20 seconds; 32 cycles of 98°C for 20 seconds, 72°C for 25 seconds; 72°C for 5 minutes. Additionally, the final combined library was gel isolated from a polyacrylamide gel to remove primer dimers.

Standard Illumina multiplex adapters were ligated to RHOX bisulfite PCR amplicons and to *HBB* PCR amplicons #1 and 2 and indexes were added by PCR as described below.

RHOXF2 PCR Conditions #1(for -600 to -800 region)

Initial amplification was performed on 4 µl bisulfite-treated genomic DNA in a 50 µl reaction using Pyromark PCR kit (Qiagen) according to the manufacturer's protocol with the following PCR conditions: 95°C for 15 minutes; 45 cycles of 94°C for 30 seconds, 64°C for 30 seconds, 72°C for 30 seconds; 72°C for 10 minutes. PCR was purified with Agencourt AMpure XP PCR purification beads (Beckman Coulter). End repair was performed with a combination of T4 DNA polymerase, Klenow DNA polymerase and T4 polynucleotide kinase (NEB) and A-tailing was performed with Klenow (3' to 5' exo-) and 200 nM dATP (NEB). Standard Illumina multiplex adapters were ligated using T4 DNA ligase (NEB) and final product was purified using AMpure XP. Approximately 5-10 ng of purified adapter-ligated initial PCR was used as template for PCR with Illumina Multiplexing PCR primer 1.0 and Illumina Multiplexing PCR primer 2.0 (**Supplementary Table 1**) using a Pyromark PCR kit (Qiagen) and the following PCR conditions: 95°C for 15 minutes; 6 to 10 cycles (depending on template concentration) of 94°C

for 20 seconds, 65°C for 30 seconds, 72°C for 30 seconds; 72°C for 5 minutes. PCR was purified with Agencourt AMpure XP PCR purification beads (Beckman Coulter) and quantified on a QIAxcel (Qiagen). 1 ng of purified PCR was used as template for PCR with Illumina Multiplexing PCR primer 1.0 and one of 60 Illumina Index primers (**Supplementary Table 1**) using Pyromark PCR kit and the following PCR conditions: 95°C for 15 minutes; 10 of 94°C for 20 seconds, 57°C for 30 seconds, 72°C for 30 seconds; 72°C for 5 minutes. PCR was purified with Agencourt AMpure XP PCR purification beads (Beckman Coulter), quantified on a QIAxcel (Qiagen) and equal molar amounts of each amplicon were combined. The final combined library was gel isolated from a polyacrylamide gel to remove primer dimers.

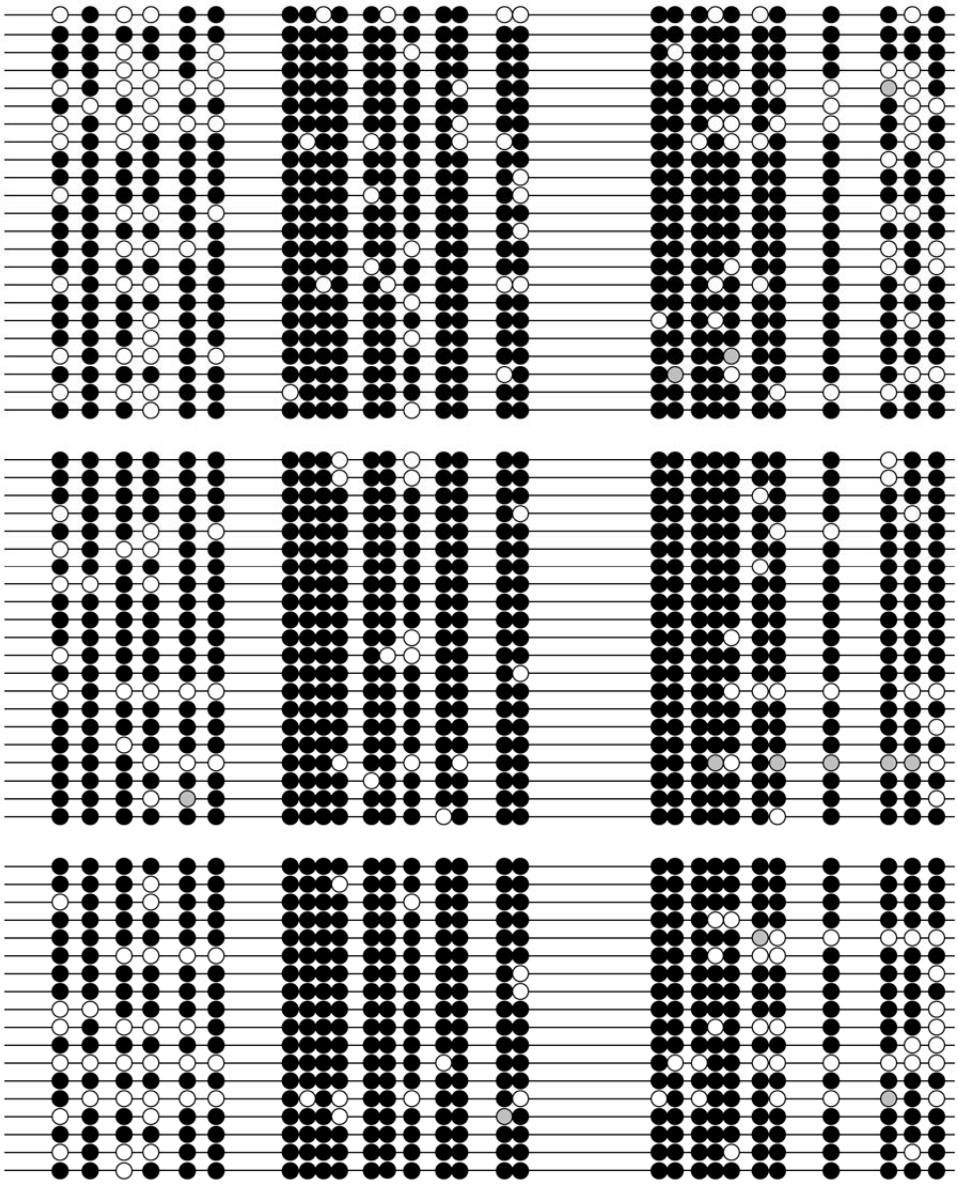
RHOXF2 PCR Conditions #2 (for +1 to -200 region)

Exactly as described for RHOXF2 PCR Conditions #1 but with the following PCR conditions for initial amplification: 95°C for 15 minutes; 45 cycles of 94°C for 30 seconds, 62°C for 30 seconds, 72°C for 30 seconds; 72°C for 10 minutes.

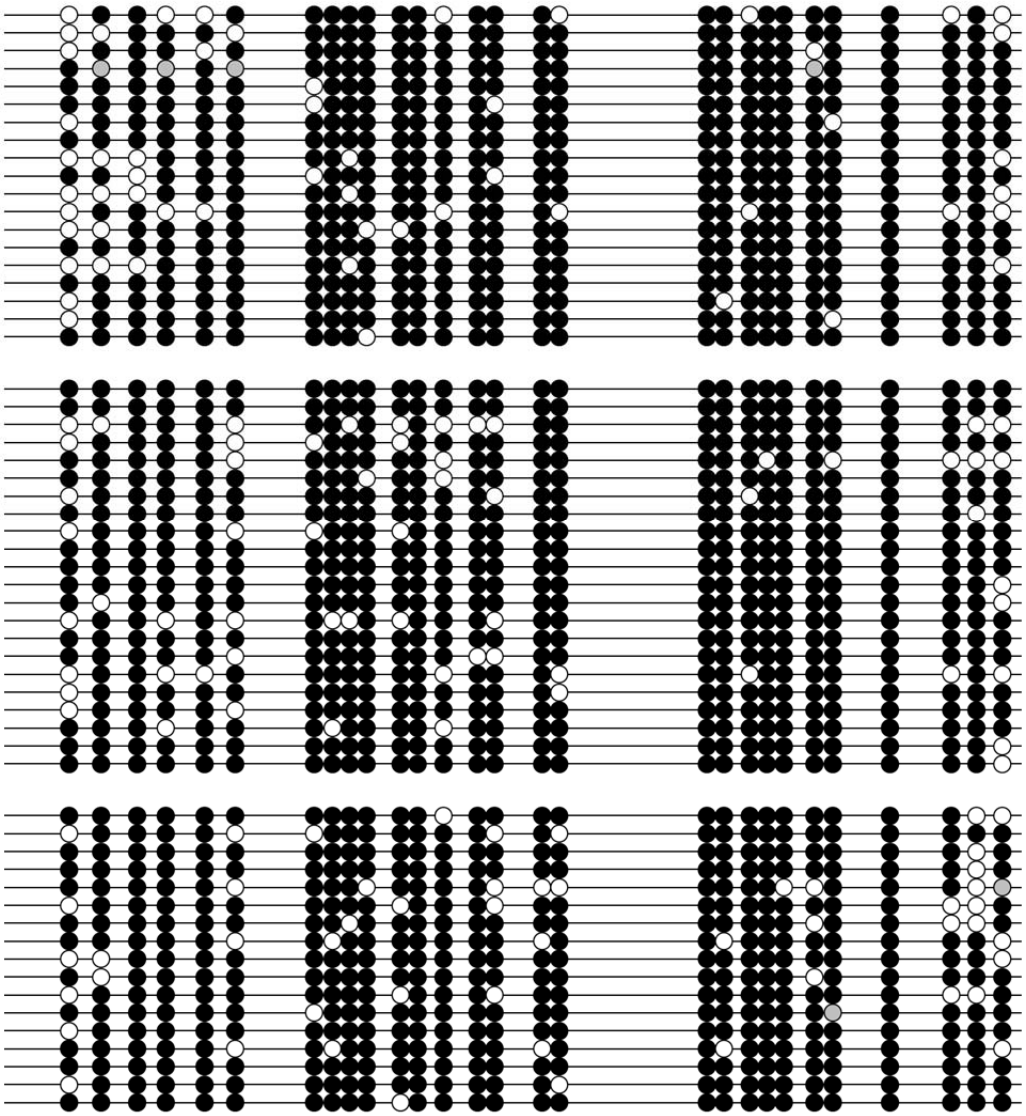
HBB PCR Conditions #1 (for -415, -307 and -266 CpGs) and #2 (for -126, +83 and +110 CpGs)

Exactly as described for RHOXF2 PCR Conditions #1 but initial PCR was performed on 1ul bisulfite-treated DNA template in a 40ul PCR reaction with KAPA HiFi HotStart Uracil+ ReadyMix and the following PCR conditions: 95°C for 5 minutes; 10 cycles of 98°C for 20 seconds, 63.2°C for 15 seconds, 72°C for 20 seconds; 32 cycles of 98°C for 20 seconds, 72°C for 25 seconds; 72°C for 5 minutes. PCR reactions with Illumina multiplexing primers were performed as described for RHOXF2 but with with Phusion Hot Start Flex DNA polymerase (NEB) and an initial denaturation step of 98° for 2 minutes.

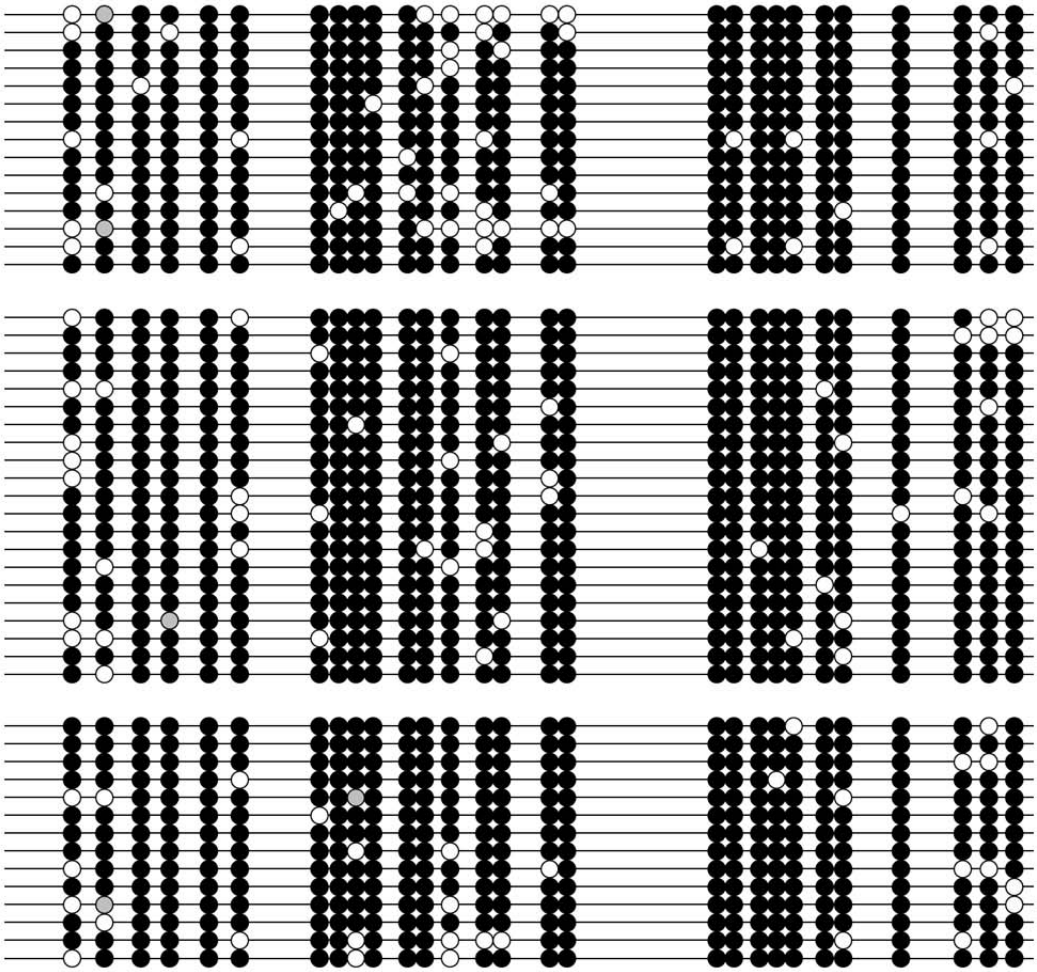
A KL-1 TALE-TET1



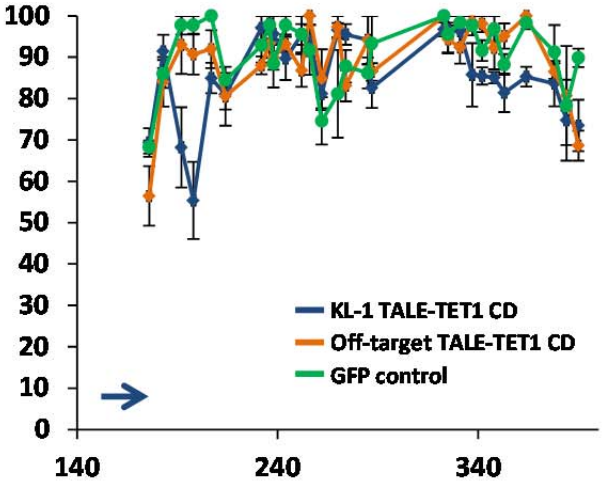
B Off-target TALE-TET1



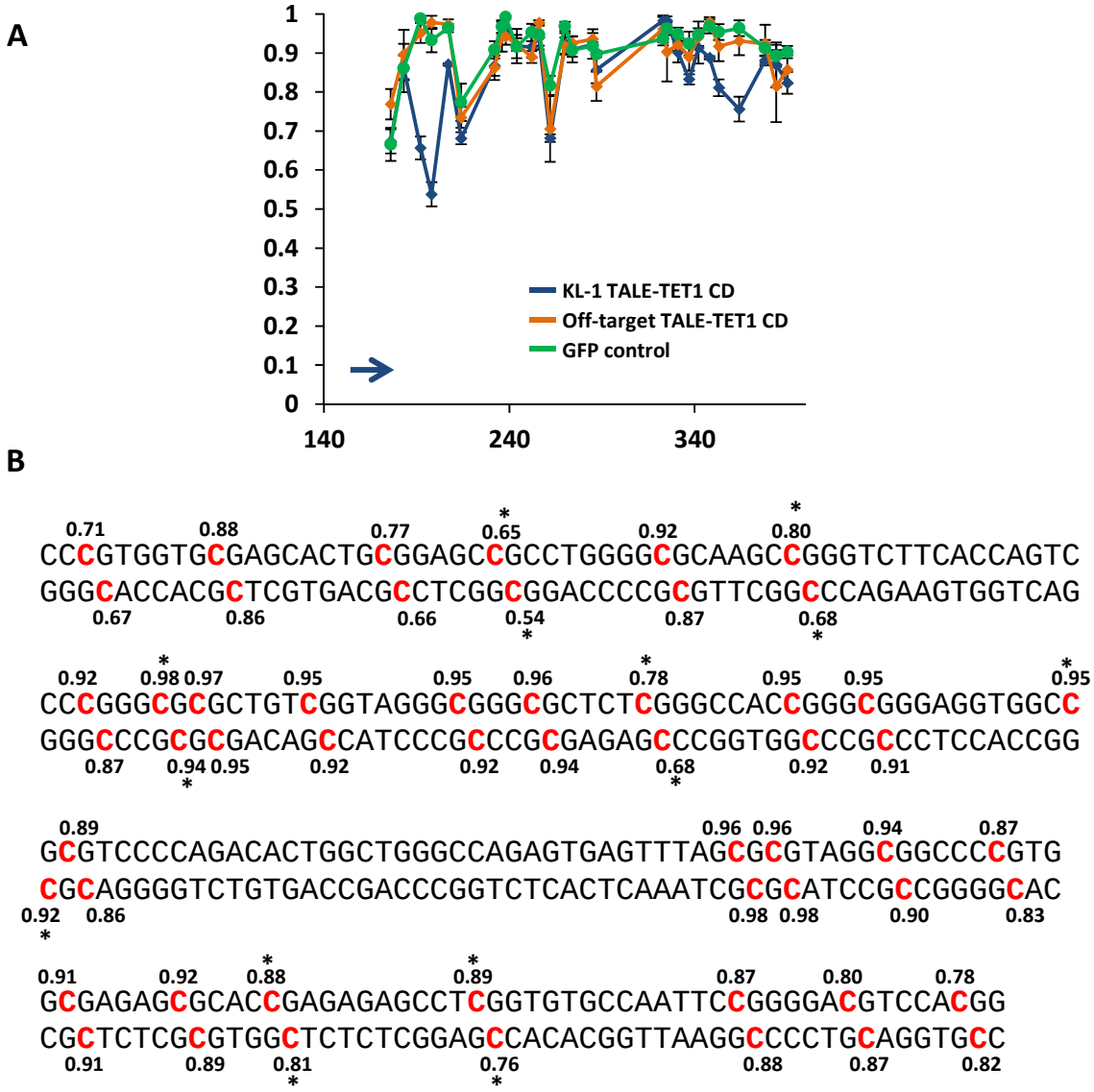
C GFP control



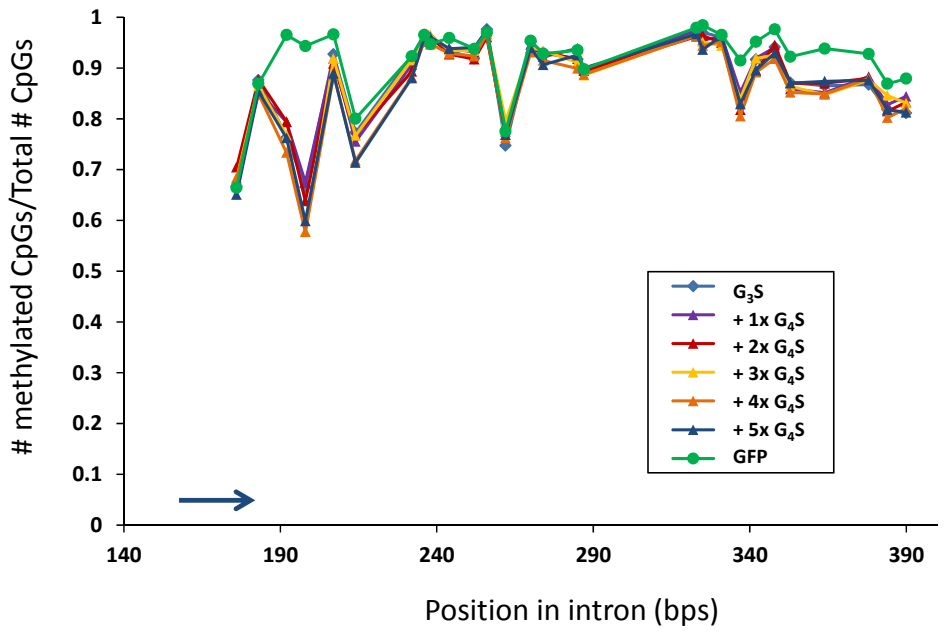
D



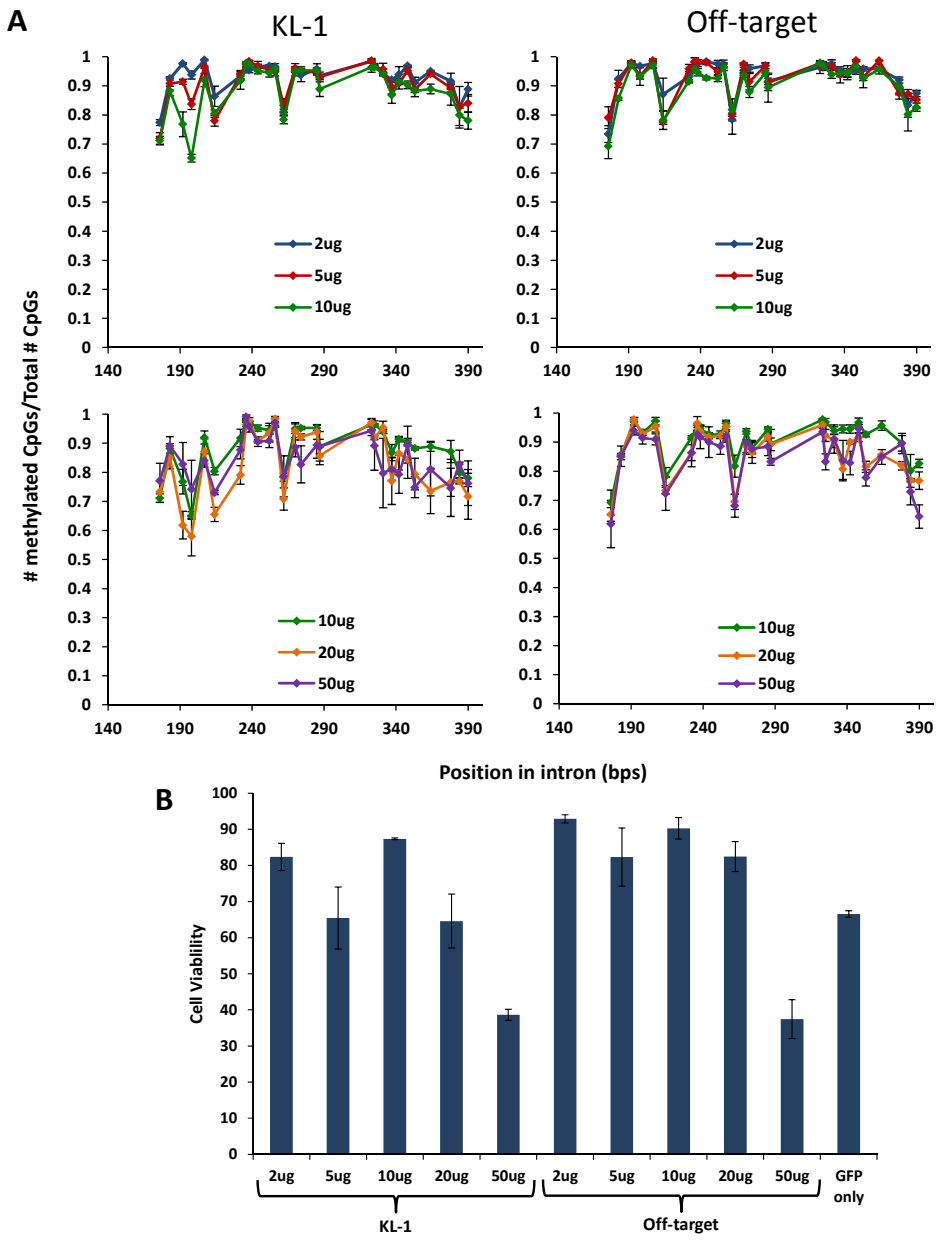
Supplementary Figure 1 Sanger sequencing of bisulfite PCR products. Figures depict methylation status of CpGs in the second *KLF4* intron in K562 cells transfected with plasmid expressing (a) the KL-1 TALE-TET1 fusion, (b) an off-target TALE-TET1 fusion (targeted to a sequence in the EGFP reporter gene), or (c) GFP. Genomic DNA is the same as that used in the 10 ug sample in Supplementary Fig. 1a and in Supplementary Fig. 2. Each panel shows three sets of sequences derived from three independent transfections. Black circles, methylated; white circles, non-methylated; grey circles, undetermined. (d) Summary of data from (a), (b), and (c) showing the fraction of methylated CpGs (y-axis) for different positions along the length of the second *KLF4* intron (x-axis, numbered relative to the start of the intron).



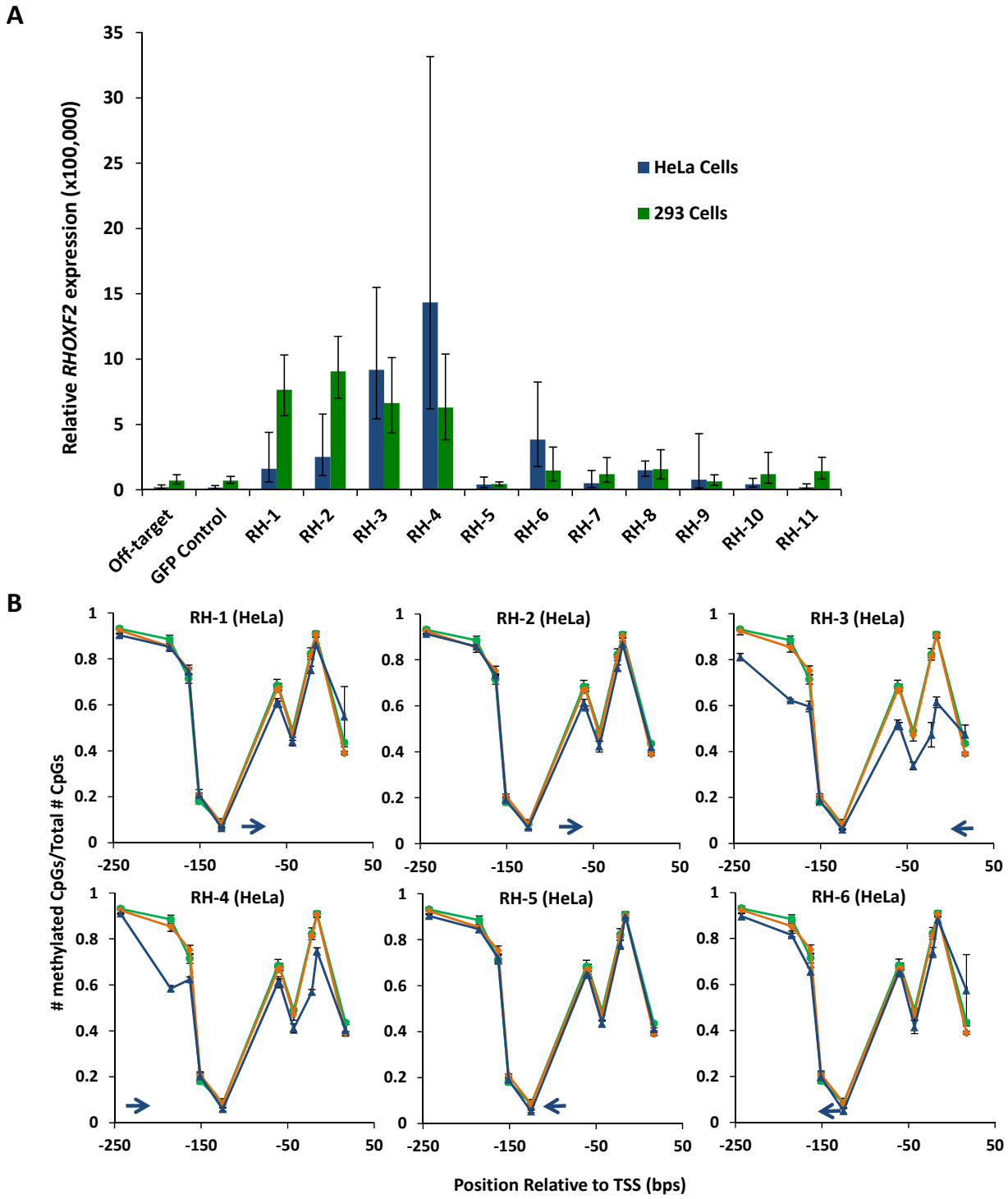
Supplementary Figure 2 TALE-TET1 fusion protein can induce demethylation of both DNA strands. (a) Graph shows the fraction of CpGs methylated (y-axis) for different positions along the length of the second *KLF4* intron (x-axis, numbered relative to the start of the intron) in K562 cells transfected with plasmid expressing KL-1 TALE-TET1 (blue), an off-target TALE-TET1 fusion protein (orange) or a GFP (control). Genomic DNA is the same as in **Fig. 1d** except that bisulfite PCR was performed to amplify the opposite DNA strand. (b) Schematic summary of mean CpG methylation at the KL-1 target locus from K562 cells transfected with plasmid encoding the KL-1 TALE-TET1 fusion protein. Data for this figure is derived from **Fig. 1d** (for the top strand) and **Supplementary Fig. 2a** (for the bottom strand). CpGs that have significantly different rates of methylation on the two strands in the KL-1 TALE-TET1 samples are indicated by asterisks, as determined by a two-sided t-test (n=3, $p<0.05$). No significant differences between methylation rates on the two strands were observed for cells transfected with plasmid encoding the off-target TALE-TET1 fusion protein or GFP (data not shown).

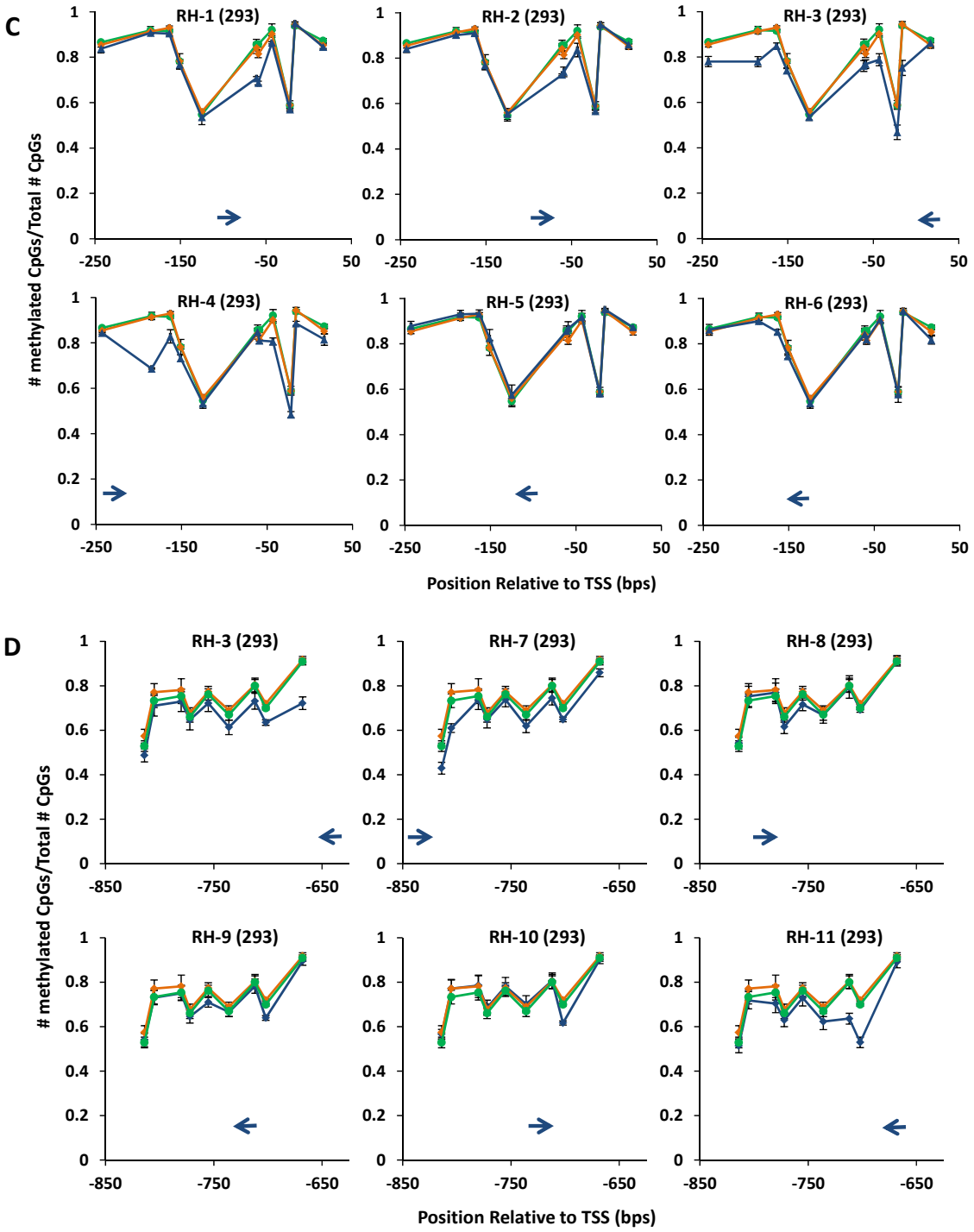


Supplementary Figure 3 CpG demethylation induced by TALE-TET1 fusion proteins bearing various length inter-domain linkers. Graphs show the fraction of CpGs methylated (y-axis) for different positions along the length of the second *KLF4* intron (x-axis, numbered relative to the start of the intron) in K562 cells transfected with plasmids expressing KL1 TALE-TET1 proteins bearing standard or variant linkers between the TALE and TET1 domains or a control plasmid expressing GFP. Blue arrow indicates the location and direction (5' to 3') of TALE target binding site. Each point represents data from a single transfection experiment. Methylation status was assessed using high-throughput bisulfite sequencing.



Supplementary Figure 4 Titration of TALE-TET1 plasmid. (a) Fraction of CpGs methylated (y-axis) for different positions along the length of the second *KLF4* intron (x-axis, numbered relative to the start of the intron) in K562 cells transfected with indicated amounts of plasmid expressing KL-1 TALE-TET1 (left) or an off-target TALE-TET1 fusion protein targeted to an unrelated sequence in the *EGFP* reporter gene (right). Each point represents the mean of three independent transfection experiments with bars indicating standard errors of the mean. Methylation status for each experiment was assessed using high-throughput bisulfite sequencing. Note that 10ug samples are the same in top and bottom graphs and are depicted twice for ease of comparison. 10ug samples are also the same as those depicted in Fig. 1d and genomic DNA is the same as that used in **Supplementary Fig. 2**. (b) Cell viability of transfected K562 cells from (a) as determined by propidium iodide standing and FACS.


A
Relative RHOXF2 expression (x100,000)
35
30
25
20
15
10
5
0
HeLa Cells
293 Cells
Off-target
GFP Control
RH-1
RH-2
RH-3
RH-4
RH-5
RH-6
RH-7
RH-8
RH-9
RH-10
RH-11
B
RH-1 (HeLa)
RH-2 (HeLa)
RH-3 (HeLa)
RH-4 (HeLa)
RH-5 (HeLa)
RH-6 (HeLa)
methylated CpGs/Total # CpGs
1
0.8
0.6
0.4
0.2
0
-250
-150
-50
50
Position Relative to TSS (bps)


C
RH-1 (293)
RH-2 (293)
RH-3 (293)
RH-4 (293)
RH-5 (293)
RH-6 (293)
methylated CpGs/Total # CpGs
Position Relative to TSS (bps)
D
RH-3 (293)
RH-7 (293)
RH-8 (293)
RH-9 (293)
RH-10 (293)
RH-11 (293)
methylated CpGs/Total # CpGs
Position Relative to TSS (bps)

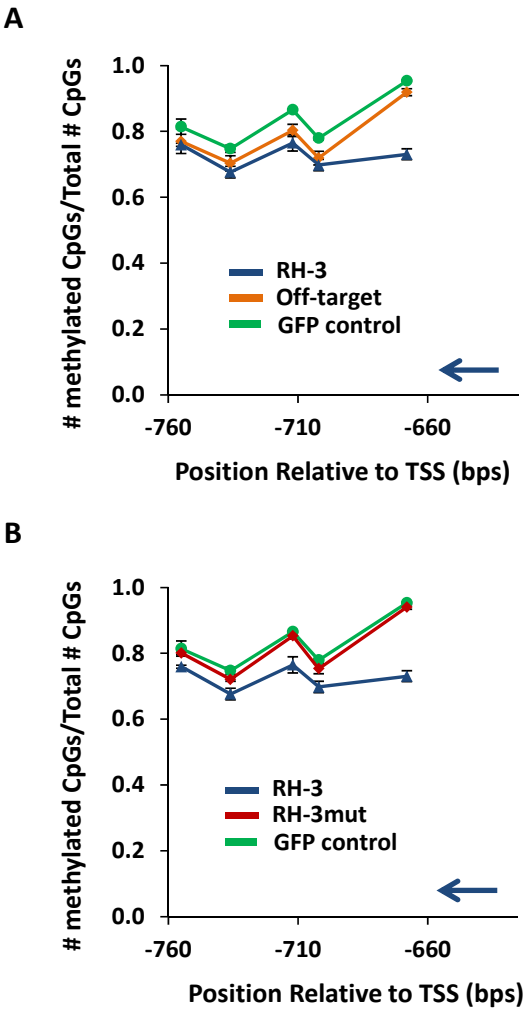
Supplementary Figure 5 Targeted demethylation and activation of the *RHOXF2* gene.

(a) Expression levels of *RHOXF2* mRNA (normalized to β-actin mRNA levels) as determined by quantitative RT-PCR in HeLa (blue) and 293 (green) cells transfected with plasmids encoding one of 11 different TALE-TET1 fusion proteins (RH-1 to RH-11), an off-target control (targeted to *KLF4*) or a GFP control. Means of three independent replicates are shown with error bars representing standard errors of the mean.

(b) Fraction of methylated CpGs (y-axis) for different positions within the -200 to +1 region of the *RHOXF2* promoter (x-axis, numbered relative to the transcription start site) in HeLa cells transfected with plasmids expressing *RHOXF2*-targeted TALE-TET1 proteins (blue), an off-target TALE-TET1 protein (targeted to a site in the *KLF4* gene) (orange), or GFP (green). Means of three independent transfection experiments are shown with bars representing standard errors of the mean. Methylation status for each experiment was assessed using high-throughput bisulfite sequencing. Note that the GFP and off-target TALE-TET1 control data points shown are the same in panels (c) and (d) and are depicted multiple times only for ease of comparison with experimental samples. Blue arrow indicates the location and direction (5' to 3' TALE-TET1 binding sites.

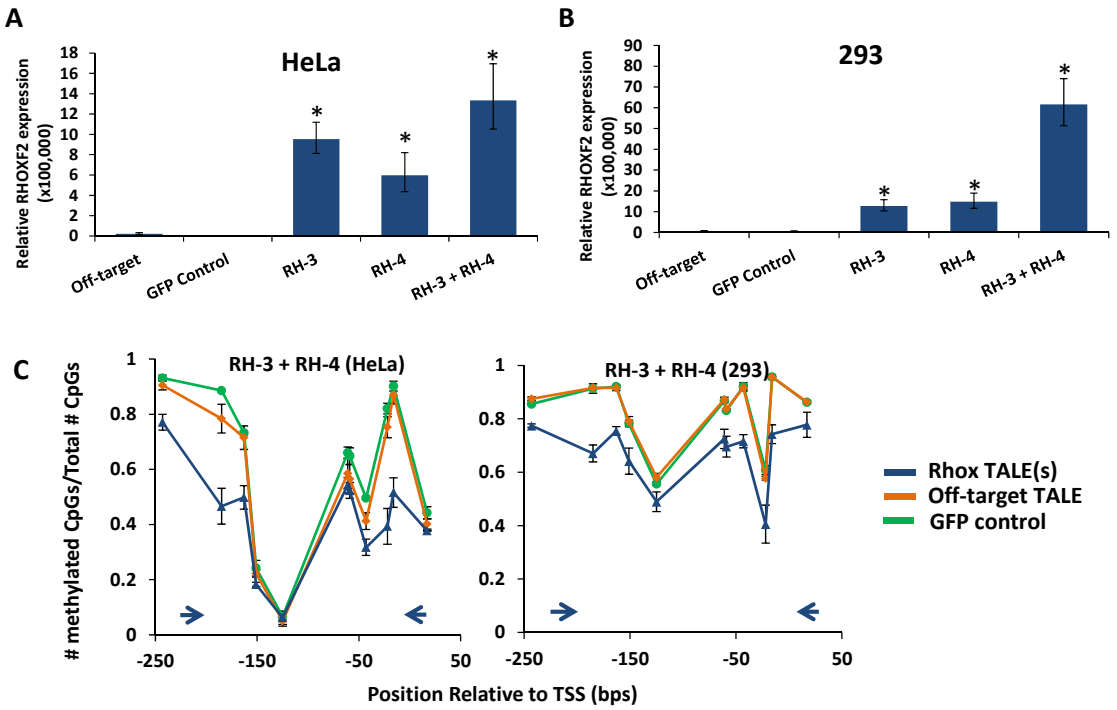
(c) Fraction of methylated CpGs for various positions within the -200 to +1 region of the RHOXF2 promoter in 293 cells transfected with plasmids expressing *RHOXF2*-targeted TALE-TET1 proteins (blue), an off-target TALE-TET1 protein (targeted to a site in the *KLF4* gene) (orange), or GFP (green). Data depicted as in (b).

(d) Fraction of methylated CpGs for various positions within the -650 to -850 region of the RHOXF2 promoter in 293 cells transfected with plasmids expressing *RHOXF2*-targeted TALE-TET1 proteins (blue), an off-target TALE-TET1 protein (targeted to a site in the *KLF4* gene) (orange), or GFP (green). Data depicted as in (b) and (c).



Supplementary Figure 6 RH-3 TALE-TET1 demethylates CpGs at its secondary upstream binding site in 293 cells.

(a) Graph shows the fraction of CpGs methylated (y-axis) for different positions along the length of the *RHOXF2* promoter (x-axis, numbered relative to the transcription start site) in cells transfected with plasmids expressing the RH-3 TALE-TET1 fusion (blue), a TALE-TET1 fusion targeted to an off-target site in the KLF4 gene (orange), or GFP (green). Each data point represents the mean of three independent transfection experiments with bars indicating standard errors of the mean. Methylation status for each experiment was assessed using high-throughput bi-sulfite sequencing. Blue arrow indicates the location and direction (5' to 3') of the RH3 TALE-TET1 binding site. (b) Same as in (a) but showing data from cells transfected with plasmid encoding RH-3 TALE-TET1 fusion (blue), RH-3 TALE-TET1 fusion bearing mutations to inactivate the catalytic activity of TET1 (red), or GFP (green).Note that the data for the RH-3 TALE-TET1 and GFP samples are the same in both (a) and (b) and are depicted twice only for ease of comparison.

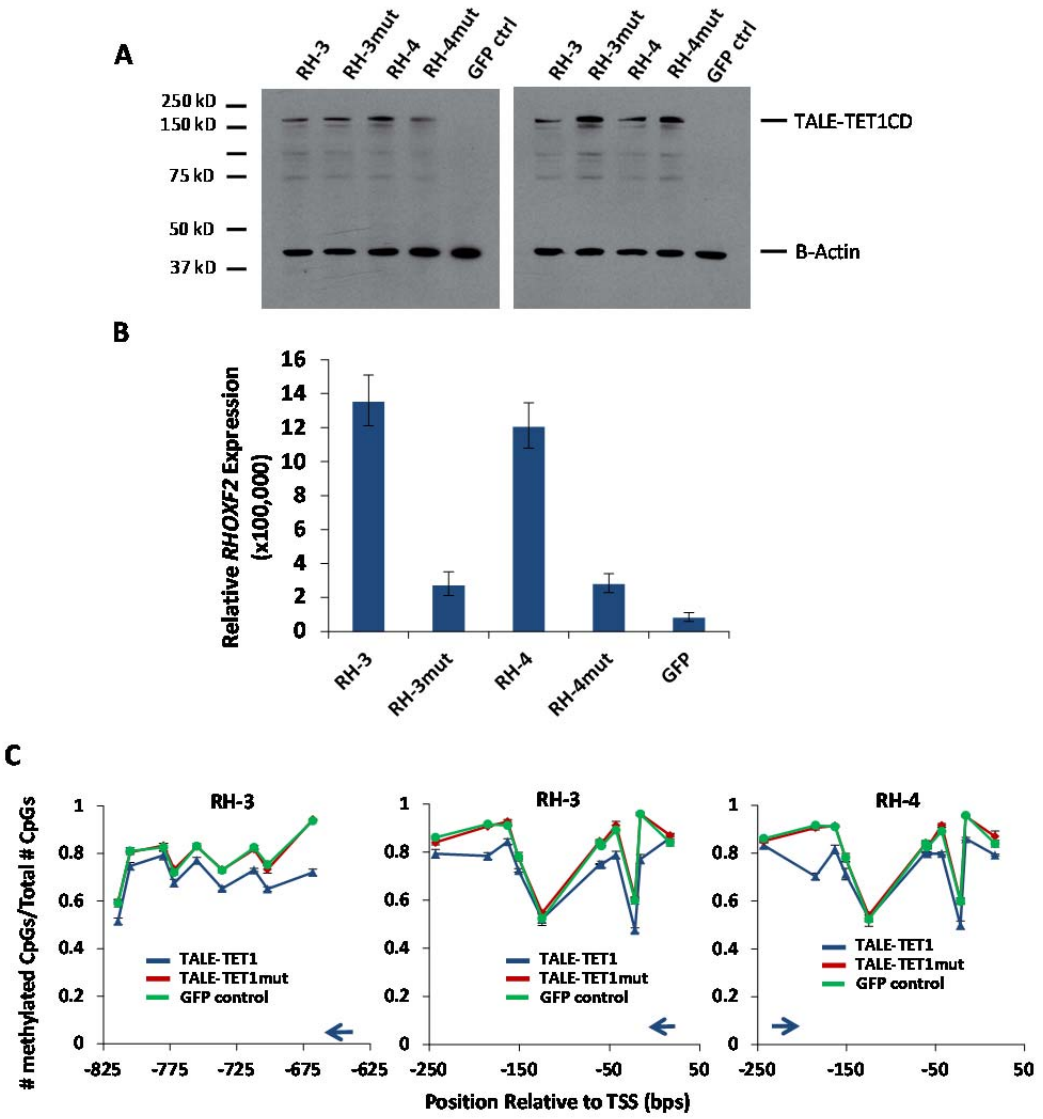


Supplementary Figure 7 Co-expression of RH-3 and RH-4 TALE-TET1 proteins.

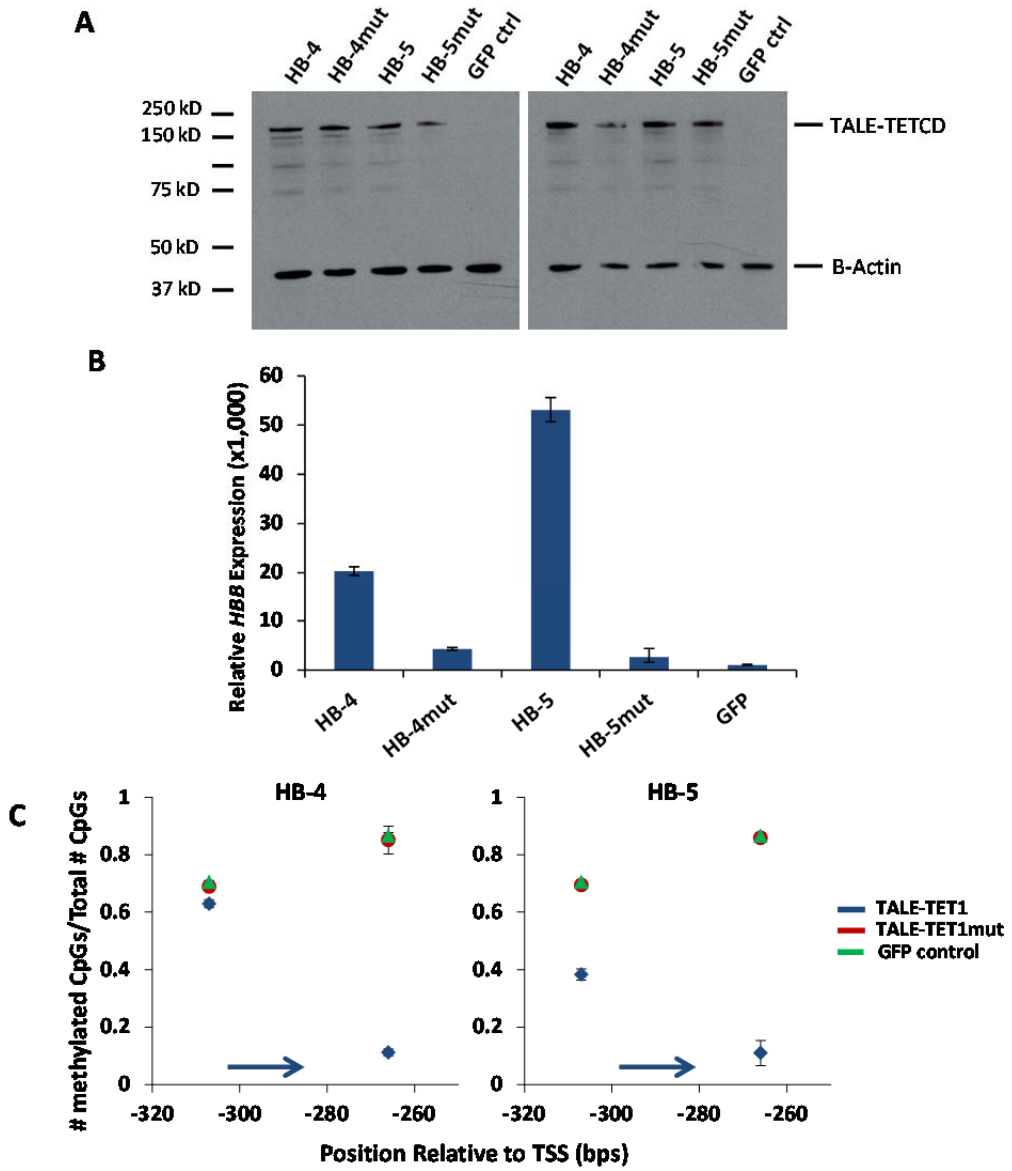
(a) Expression levels of *RHOXF2* mRNA (normalized to β-actin mRNA levels) in HeLa cells transfected with plasmids expressing RH-3, RH-4, or both TALE-TET1 proteins, an off-target TALE-TET1 protein (targeted to *KLF4*), or GFP. Means of three independent transfection samples each assayed three times by quantitative RT-PCR are shown with bars representing standard errors of the mean. Asterisks indicate samples with values significantly greater than those obtained with the off-target control TALE-TET1 fusion protein as determined by a one-sided Welch's t-test ($n = 3$, $p<0.05$).

(b) Expression levels of *RHOXF2* mRNA (normalized to β-actin mRNA levels) in 293 cells transfected with plasmids expressing RH-3, RH-4, or both TALE-TET1 proteins, an off-target TALE-TET1 protein (targeted to *KLF4*) or GFP expression. Data presented as in (a).

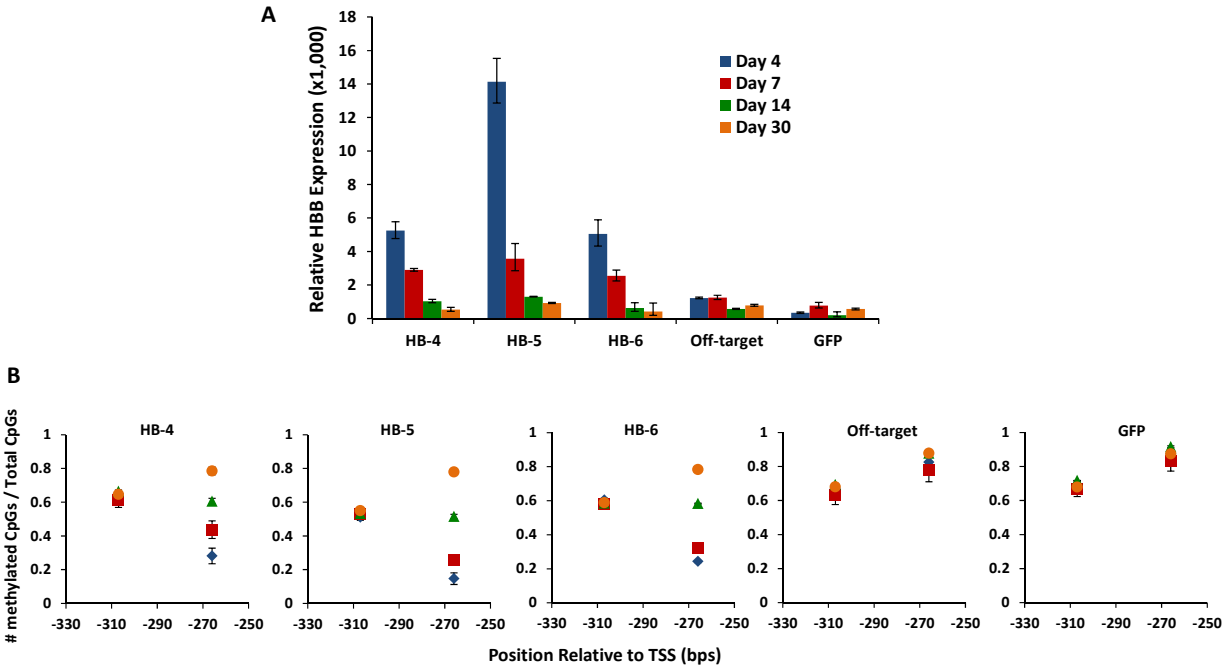
(c) Fraction of methylated CpGs (y-axis) for different positions along the length of the *RHOXF2* promoter (x-axis, numbered relative to the transcription start site) in HeLa (left) and 293 (right) cells transfected with plasmids expressing RH-3, RH-4, or both (blue), an off-target TALE-TET1 fusion (to a site in the *KLF4* gene) (orange), or GFP (green). Each data point represents the mean of three independent transfection experiments with bars indicating standard errors of the mean. Methylation status for each experiment was assessed using high-throughput bisulfite sequencing. Blue arrow indicates the location and direction (5' to 3') of the RH3 (right) and/or RH4 (left) TALE-TET1 binding sites.



Supplementary Figure 8 *RhoxF2*-targeted TALE-TET1 proteins bearing mutations that inactivate TET1 catalytic function are stably expressed in 293 cells.
(a) Western blot analysis performed on 293 cells transfected with plasmids expressing triple-FLAG-tagged RH-3 or RH-4 TALE-TET1 fusions, FLAG-tagged RH-3 or RH-4 TALE-TET1 fusions bearing mutations that inactivate TET1 catalytic function, or GFP. Transfections were performed in triplicate and Western blots performed for two replicates using anti-FLAG antibody are shown. (b) Expression levels of *RHOXF2* mRNA (normalized to β-actin mRNA levels) from the same transfected cells described in (a). Means of three independent samples each assayed three times by quantitative RT-PCR are shown with bars representing standard errors of the mean. (c) Fraction of CpGs methylated (y-axis) for different positions along the length of the *RHOXF2* promoter (x-axis, numbered relative to the transcription start site) for the same transfected cells described in (a). Each data point represents the mean of the three independent transfection experiments with bars indicating standard errors of the mean. Methylation status for each experiment was assessed using high-throughput bisulfite sequencing. Note that the control GFP data in the second and third panels are the same and are presented twice for ease of comparison.



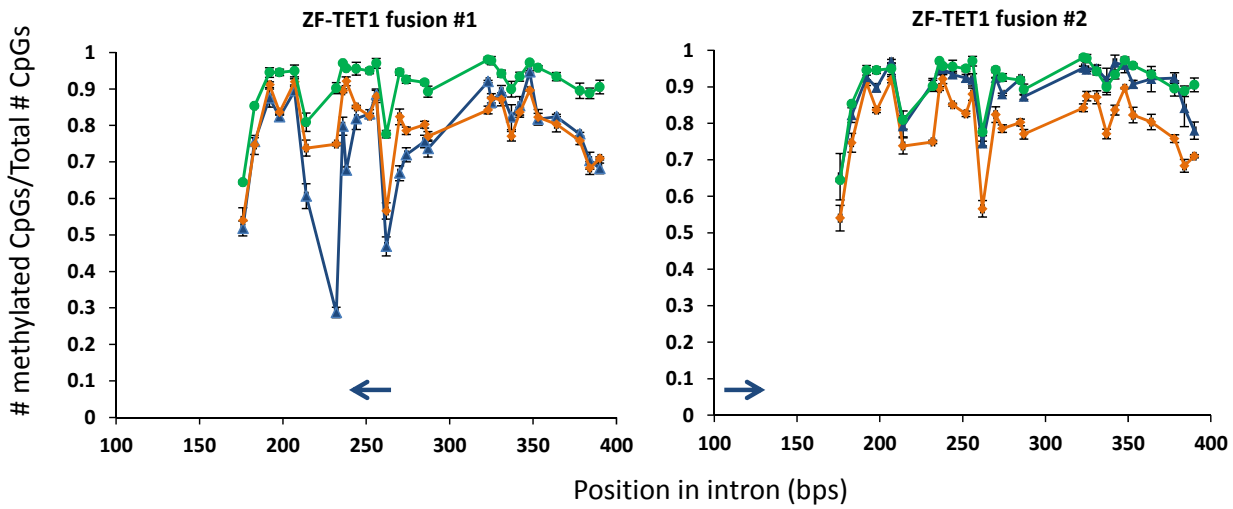
Supplementary Figure 9 *HBB*-targeted TALE-TET1 proteins bearing mutations that inactivate TET1 catalytic domain function are stably expressed in K562 cells.
(a) Western blot analysis performed on K562 cells transfected with plasmids expressing triple-FLAG epitope-tagged HB-4 or HB-5 TALE-TET1 fusions, HB-4 or HB-5 TALE-TET1 fusions bearing mutations that inactivate TET1 catalytic function, or GFP. Transfections were performed in triplicate and Western blots performed for two replicates using anti-FLAG antibody are shown. (b) Expression levels of *HBB* mRNA (normalized to β-actin mRNA levels) from the same transfected cells described in (a). Means of three independent samples assayed by quantitative RT-PCR are shown with bars representing standard errors of the mean.
(c) Fraction of CpGs methylated (y-axis) for different positions along the length of the *HBB* promoter (x-axis, numbered relative to the transcription start site) for the same transfected cells described in (a). Each data point represents the mean of the three independent transfection experiments with bars indicating standard errors of the mean. Methylation status for each experiment was assessed using high-throughput bisulfite sequencing. Note that the control GFP data in the left and right panels are the same and are presented twice for ease of comparison.



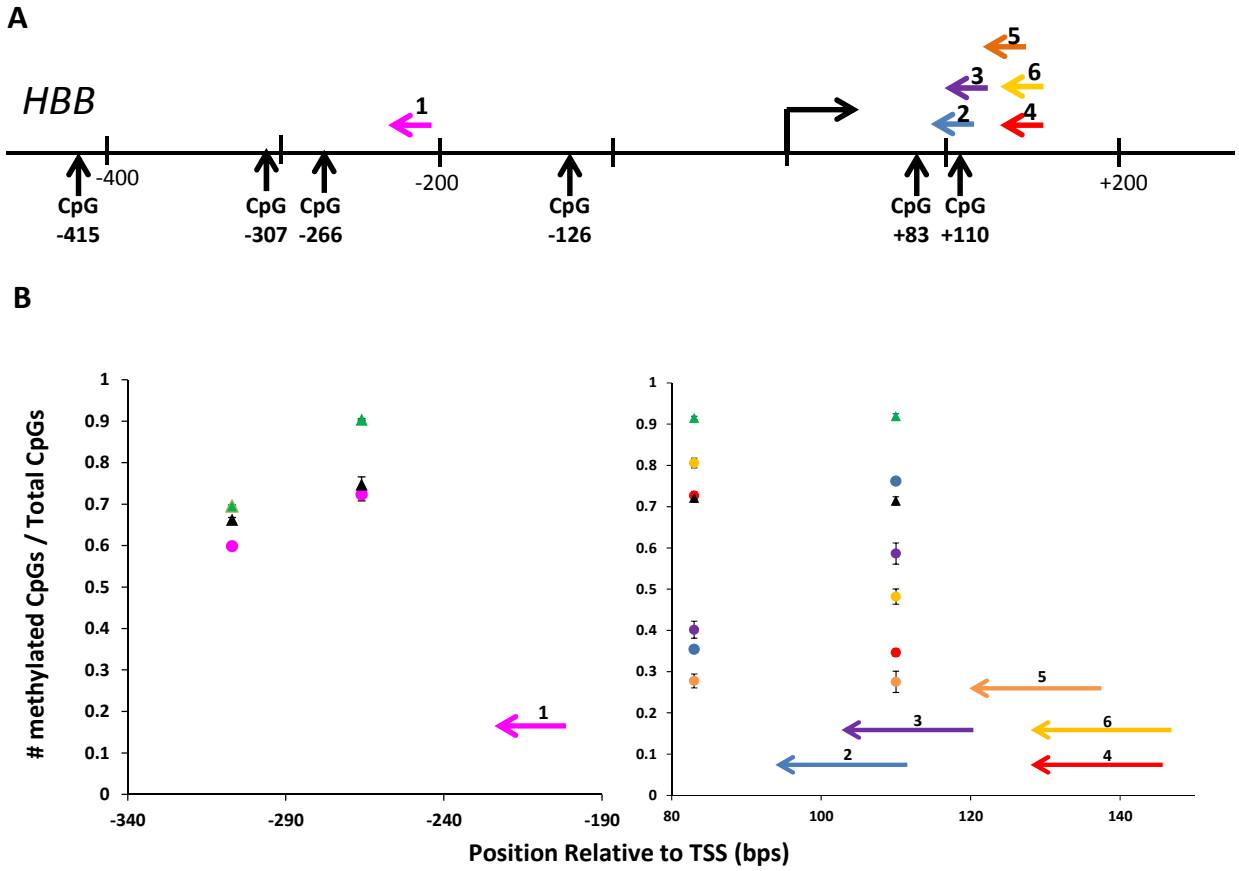
Supplementary Figure 10 Extended time-course experiment assessing promoter CpG methylation and expression of the human *HBB* gene in cells transfected with plasmids expressing TALE-TET1 fusion proteins

(a) Expression levels of *HBB* mRNA (normalized to β-actin mRNA levels) in K562 cells transfected with plasmids expressing HB-4, HB-5, HB-6, an off-target TALE-TET1 fusion protein (targeted to the human *KLF4* gene), or GFP were measured 4, 7, 14, and 30 days post-transfection. Means of three independent samples assayed by quantitative RT-PCR are shown with bars representing standard errors of the mean.

(b) Graphs showing the fraction of CpGs methylated (y-axis) for different positions along the length of the *HBB* promoter (x-axis, numbered relative to the transcription start site) for the same transfected cells described in (a). Each data point represents the mean of the three independent transfection experiments with bars indicating standard errors of the mean. Methylation status for each experiment was assessed using high-throughput bisulfite sequencing.



Supplementary Figure 11 ZF-TET1 fusion protein-induced demethylation of the human *KLF4* gene. Fraction of CpGs methylated (y-axis) for different positions along the length of the second *KLF4* intron (x-axis, numbered relative to the start of the intron) are shown for K562 cells transfected with plasmids expressing one of two *KLF4*-targeted ZF-TET1 fusions, an off-target ZF-TET1 fusion (targeted to an unrelated site in the human *VEGFA* gene), or GFP. Blue arrows indicate the location and direction (3' to 5') of the ZF target binding sites. Each point represents the mean of three independent transfection experiments with bars indicating standard errors of the mean. Methylation status for each experiment was assessed using high-throughput bisulfite sequencing. Note that the off-target ZF-TET1 fusion and GFP control data shown are the same for both graphs and are depicted twice for ease of comparison.



Supplementary Figure 12 ZF-TET1 fusion protein-induced demethylation of the human *HBB* gene.
(a) Schematic illustrating the human *HBB* locus with CpGs indicated with black arrows. Numbering indicates position on the DNA relative to the start site of transcription (right-angle arrow). Colored arrows indicate the location and direction (3' to 5') of six ZF-TET1 fusion protein binding sites.
(b) Fraction of CpGs methylated (y-axis) for different positions along the length of *HBB* gene (x-axis, numbered relative to *HBB* promoter transcription start site) for K562 cells transfected with plasmids expressing one of six *HBB*-targeted ZF-TET1 fusions (colored circles corresponding to colored arrows in (a)), an off-target ZF-TET1 fusion (targeted to an unrelated site in the human *VEGFA* gene) (black triangles), or GFP (green triangles). Colored arrows indicate the position, location and direction (3' to 5') of the ZF target binding sites. Data for ZF-TET1 proteins targeted to the -266 and +83/+110 CpGs are shown in the left and right panels, respectively. Each point represents the mean of three independent transfection experiments with bars indicating standard errors of the mean. Methylation status for each experiment was assessed using high-throughput bisulfite sequencing.

Supplementary Figure 13. Amino acid sequences of fusion proteins used in this work

Sequence of TALE-TET1CD Backbone (includes NLS, TALE N-terminal domain, TALE-C-terminal domain, TET1 catalytic domain):

MAPKKKRKVGIHRGVPMVDLRTLGYSQQQQEKIKPKVRSTVAQHHEALVGHGFTHAHIVALSQHPAALGTVAVKYQD
MIAALPEATHEAIVGVGKQWSGARALEALLTVAGELRGPPLQLDTGQLLKIAKRGGVTAVEAVHAWRNALTGAPLN
…Insert TALE Repeat Arrays Here (see below) …
SIVAQLSRPDPALAALTNDHLVALACLGGRPALDAVKKGLPHAPALIKRTNRRIPERTSHRVADHAQVVRVLGFFQCHS
HPAQAFDDAMTQFGMSGGGSLPTCSCLDRVIQKDKGPYYTHLGAGPSVAAVREIMENRYGQKGNAIRIEIVVYTGKE
GKSSHGCPIAKWVLRRSSDEEKVLCLVRQRTGHHCPTAVMVVLIMVWDGIPLPMADRLYTELTENLKSYNGHPTDRRC
TLNENRTCTCQGIDPETCGASFSFGCSWSMYFNGCKFGRSPSPRRFRIDPSSPLHEKNLEDNLQSLATRLAPIYKQYAPV
AYQNQVEYENVARECRLGSKEGRPFSGVTACLDFCAHPHRDIHNMNNGSTVVCTLTREDNRSLGVIPQDEQLHVLPLY
KLSDTDEFGSKEGMEAKIKSGAIEVLAPRRKKRTCFTQPVPRSGKKRAAMMTEVLAHKIRAVEKKPIPRIKRKNNSTTTN
NSKPSSLPTLGSNTETVQPEVKSETEPHFILKSSDNTKTYSLMPSAPHPVKEASPGFSWSPKTASATPAPLKNDATASCGF
SERSSTPHCTMPSGRLSGANAAAADGPGISQLGEVAPLPTLSAPVMEPLINSEPSTGVTEPLTPHQPNHQPSFLTSPQDL
ASSPMEEDEQHSEADEPPSDEPLSDDPLSPAEEKLPHIDEYWSDSEHIFLDANIGGVAIAPAHGSVLIECARRELHATTPV
EHPNRNHPTRLSLVFYQHKNLNKPQHGFELNKIKFEAKEAKNKKMKASEQKDQAANEGPEQSSEVNELNQIPSHKALT
LTHDNVVTVSPYALTHVAGPYNHWV.

Sequence of TALE-TET1FL Backbone (includes NLS, TALE N-terminal domain, TALE-C-terminal domain, full length TET1):

MAPKKKRKVGIHRGVPMVDLRTLGYSQQQQEKIKPKVRSTVAQHHEALVGHGFTHAHIVALSQHPAALGTVAVKYQD
MIAALPEATHEAIVGVGKQWSGARALEALLTVAGELRGPPLQLDTGQLLKIAKRGGVTAVEAVHAWRNALTGAPLN
…Insert TALE Repeat Arrays Here (see below)…
SIVAQLSRPDPALAALTNDHLVALACLGGRPALDAVKKGLPHAPALIKRTNRRIPERTSHRVADHAQVVRVLGFFQCHS
HPAQAFDDAMTQFGMSGGGSMSRSRHARPSRLVRKEDVNKKKKNSQLRKTTKGANKNVASVKTLSPGKLKQLIQER
DVKKKTEPKPPVPVRSLLTRAGAARMNLDRTEVLFQNPESLTCNGFTMALRSTSLSRRLSQPPLVVAKSKKVPLSKGLEK
QHDCDYKILPALGVKHSENDSVPMQDTQVLPDIETLIGVQNPSLLKGKSQETTQFWSQRVEDSKINIPTHSGPAAEILPG
PLEGTRCGEGLFSEETLNDTSGSPKMFAQDTVCAPFPQRATPKVTSQGNPSIQLEELGSRVESLKLSDSYLDPIKSEHDCY
PTSSLNKVIPDLNLRNCLALGGSTSPTSVIKFLLAGSKQATLGAKPDHQEAFEATANQQEVSDTTSFLGQAFGAIPHQWE
LPGADPVHGEALGETPDLPEIPGAIPVQGEVFGTILDQQETLGMSGSVVPDLPVFLPVPPNPIATFNAPSKWPEPQSTV
SYGLAVQGAIQILPLGSGHTPQSSSNSEKNSLPPVMAISNVENEKQVHISFLPANTQGFPLAPERGLFHASLGIAQLSQA
GPSKSDRGSSQVSVTSTVHVVNTTVVTMPVPMVSTSSSSYTTLLPTLEKKKRKRCGVCEPCQQKTNCGECTYCKNRKNS
HQICKKRKCEELKKKPSVVVPLEVIKENKRPQREKKPKVLKADFDNKPVNGPKSESMDYSRCGHGEEQKLELNPHTVEN
VTKNEDSMTGIEVEKWTQNKKSQLTDHVKGDFSANVPEAEKSKNSEVDKKRTKSPKLFVQTVRNGIKHVHCLPAETNV
SFKKFNIEEFGKTLENNSYKFLKDTANHKNAMSSVATDMSCDHLKGRSNVLVFQQPGFNCSSIPHSSHSIINHHASIHNE
GDQPKTPENIPSKEPKDGSPVQPSLLSLMKDRRLTLEQVVAIEALTQLSEAPSENSSPSKSEKDEESEQRTASLLNSCKAIL
YTVRKDLQDPNLQGEPPKLNHCPSLEKQSSCNTVVFNGQTTTLSNSHINSATNQASTKSHEYSKVTNSLSLFIPKSNSSKI
DTNKSIAQGIITLDNCSNDLHQLPPRNNEVEYCNQLLDSSKKLDSDDLSCQDATHTQIEEDVATQLTQLASIIKINYIKPED
KKVESTPTSLVTCNVQQKYNQEKGTMQQKPPSSVHNNHGSSLTKQKNPTQKKTKSTPSRDRRKKKPTVVSYQENDRQ
KWEKLSYMYGTICDIWIASKFQNFGQFCPHDFPTVFGKISSSTKIWKPLAQTRSIMQPKTVFPPLTQIKLQRYPESAEEKV
KVEPLDSLSLFHLKTESNGKAFTDKAYNSQVQLTVNANQKAHPLTQPSSPPNQCANVMAGDDQIRFQQVVKEQLMH
QRLPTLPGISHETPLPESALTLRNVNVVCSGGITVVSTKSEEEVCSSSFGTSEFSTVDSAQKNFNDYAMNFFTNPTKNLVS
ITKDSELPTCSCLDRVIQKDKGPYYTHLGAGPSVAAVREIMENRYGQKGNAIRIEIVVYTGKEGKSSHGCPIAKWVLRRSS

DEEKVLCLVRQRTGHHCPTAVMVVLIMVWDGIPLPMADRLYTELTENLKSYNGHPTDRRCTLNENRTCTCQGIDPETC
GASFSFGCSWSMYFNGCKFGRSPSPRRFRIDPSSPLHEKNLEDNLQSLATRLAPIYKQYAPVAYQNQVEYENVARECRL
GSKEGRPFSGVTACLDFCAHPHRDIHNMNNGSTVVCTLTREDNRSLGVIPQDEQLHVLPLYKLSDTDEFGSKEGMEAKI
KSGAIEVLAPRRKKRTCFTQPVPRSGKKRAAMMTEVLAHKIRAVEKKPIPRIKRKNNSTTTNNSKPSSLPTLGSNTETVQP
EVKSETEPHFILKSSDNTKTYSLMPSAPHPVKEASPGFSWSPKTASATPAPLKNDATASCGFSERSSTPHCTMPSGRLSG
ANAAAADGPGISQLGEVAPLPTLSAPVMEPLINSEPSTGVTEPLTPHQPNHQPSFLTSPQDLASSPMEEDEQHSEADEP
PSDEPLSDDPLSPAEEKLPHIDEYWSDSEHIFLDANIGGVAIAPAHGSVLIECARRELHATTPVEHPNRNHPTRLSLVFYQ
HKNLNKPQHGFELNKIKFEAKEAKNKKMKASEQKDQAANEGPEQSSEVNELNQIPSHKALTLTHDNVVTVSPYALTHV
AGPYNHWV.

Sequence of Flag-tagged TALE-TET1CD Backbone (includes 3X FLAG, NLS, TALE N-terminal domain, TALE-C-terminal domain, TET1 catalytic domain):

MDYKDHDGDYKDHDIDYKDDDDKMAPKKKRKVGIHRGVPMVDLRTLGYSQQQQEKIKPKVRSTVAQHHEALVGHG
FTHAHIVALSQHPAALGTVAVKYQDMIAALPEATHEAIVGVGKQWSGARALEALLTVAGELRGPPLQLDTGQLLKIAKR
GGVTAVEAVHAWRNALTGAPLN
…Insert TALE Repeat Arrays Here (see below)…
SIVAQLSRPDPALAALTNDHLVALACLGGRPALDAVKKGLPHAPALIKRTNRRIPERTSHRVADHAQVVRVLGFFQCHS
HPAQAFDDAMTQFGMSGGGSLPTCSCLDRVIQKDKGPYYTHLGAGPSVAAVREIMENRYGQKGNAIRIEIVVYTGKE
GKSSHGCPIAKWVLRRSSDEEKVLCLVRQRTGHHCPTAVMVVLIMVWDGIPLPMADRLYTELTENLKSYNGHPTDRRC
TLNENRTCTCQGIDPETCGASFSFGCSWSMYFNGCKFGRSPSPRRFRIDPSSPLHEKNLEDNLQSLATRLAPIYKQYAPV
AYQNQVEYENVARECRLGSKEGRPFSGVTACLDFCAHPHRDIHNMNNGSTVVCTLTREDNRSLGVIPQDEQLHVLPLY
KLSDTDEFGSKEGMEAKIKSGAIEVLAPRRKKRTCFTQPVPRSGKKRAAMMTEVLAHKIRAVEKKPIPRIKRKNNSTTTN
NSKPSSLPTLGSNTETVQPEVKSETEPHFILKSSDNTKTYSLMPSAPHPVKEASPGFSWSPKTASATPAPLKNDATASCGF
SERSSTPHCTMPSGRLSGANAAAADGPGISQLGEVAPLPTLSAPVMEPLINSEPSTGVTEPLTPHQPNHQPSFLTSPQDL
ASSPMEEDEQHSEADEPPSDEPLSDDPLSPAEEKLPHIDEYWSDSEHIFLDANIGGVAIAPAHGSVLIECARRELHATTPV
EHPNRNHPTRLSLVFYQHKNLNKPQHGFELNKIKFEAKEAKNKKMKASEQKDQAANEGPEQSSEVNELNQIPSHKALT
LTHDNVVTVSPYALTHVAGPYNHWV

Specific TALE Repeat Array Sequences (insert into fusion protein framework sequences above):

KL-1:
LTPDQVVAIANNNGGKQALETVQRLLPVLCQDHGLTPEQVVAIASNGGGKQALETVQRLLPVLCQAHGLTPDQVVAIA
NNNGGKQALETVQRLLPVLCQAHGLTPAQVVAIASNGGGKQALETVQRLLPVLCQDHGLTPDQVVAIASNIGGKQAL
ETVQRLLPVLCQDHGLTPEQVVAIASNGGGKQALETVQRLLPVLCQAHGLTPDQVVAIANNNGGKQALETVQRLLPVL
CQAHGLTPAQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPE
QVVAIASHDGGKQALETVQRLLPVLCQAHGLTPDQVVAIANNNGGKQALETVQRLLPVLCQAHGLTPAQVVAIASNG
GGKQALETVQRLLPVLCQDHGLTPDQVVAIANNNGGKQALETVQRLLPVLCQDHGLTPEQVVAIANNNGGKQALETV
QRLLPVLCQAHGLTPDQVVAIASNGGGKQALETVQRLLPVLCQAHGLTPEQVVAIANNNGGRPALE

KL-2
LTPDQVVAIANNNGGKQALETVQRLLPVLCQDHGLTPEQVVAIANNNGGKQALETVQRLLPVLCQAHGLTPDQVVAI
ASHDGGKQALETVQRLLPVLCQAHGLTPAQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPDQVVAIASHDGGKQA
LETVQRLLPVLCQDHGLTPEQVVAIASNIGGKQALETVQRLLPVLCQAHGLTPDQVVAIANNNGGKQALETVQRLLPVL
CQAHGLTPAQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPE
QVVAIASNIGGKQALETVQRLLPVLCQAHGLTPDQVVAIANNNGGKQALETVQRLLPVLCQAHGLTPAQVVAIASNGG
GKQALETVQRLLPVLCQDHGLTPDQVVAIANNNGGKQALETVQRLLPVLCQDHGLTPEQVVAIASNGGGKQALETVQ

RLLPVLCQAHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPAQVVAIASNGGGKQALETVQRLLPVLCQDH
GLTPEQVVAIANNNGGRPALE

RH-1
LTPDQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPEQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPDQVVAIAS
NIGGKQALETVQRLLPVLCQAHGLTPAQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPDQVVAIASHDGGKQALET
VQRLLPVLCQDHGLTPEQVVAIASNIGGKQALETVQRLLPVLCQAHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQ
AHGLTPAQVVAIASNGGGKQALETVQRLLPVLCQDHGLTPDQVVAIASNGGGKQALETVQRLLPVLCQDHGLTPEQV
VAIASNIGGKQALETVQRLLPVLCQAHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPAQVVAIASHDGGK
QALETVQRLLPVLCQDHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPEQVVAIASHDGGKQALETVQRLL
PVLCQAHGLTPDQVVAIASNGGGKQALETVQRLLPVLCQAHGLTPAQVVAIASHDGGKQALETVQRLLPVLCQDHGL
TPDQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPEQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPEQVVAIAS
HDGGRPALE

RH-2
LTPDQVVAIASNGGGKQALETVQRLLPVLCQDHGLTPEQVVAIASNIGGKQALETVQRLLPVLCQAHGLTPDQVVAIAS
HDGGKQALETVQRLLPVLCQAHGLTPAQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPDQVVAIASHDGGKQALE
TVQRLLPVLCQDHGLTPEQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPDQVVAIASNGGGKQALETVQRLLPVLC
QAHGLTPAQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPEQ
VVAIASHDGGKQALETVQRLLPVLCQAHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPAQVVAIASHDG
GKQALETVQRLLPVLCQDHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPEQVVAIASHDGGKQALETVQ
RLLPVLCQAHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPAQVVAIASNIGGKQALETVQRLLPVLCQDH
GLTPDQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPEQVVAIASNIGGKQALETVQRLLPVLCQAHGLTPEQVVAIA
SHDGGRPALE

RH-3
LTPDQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPEQVVAIASNGGGKQALETVQRLLPVLCQAHGLTPDQVVAIAS
NGGGKQALETVQRLLPVLCQAHGLTPAQVVAIASNGGGKQALETVQRLLPVLCQDHGLTPDQVVAIANNNGGKQAL
ETVQRLLPVLCQDHGLTPEQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPDQVVAIASNGGGKQALETVQRLLPVL
CQAHGLTPAQVVAIANNNGGKQALETVQRLLPVLCQDHGLTPDQVVAIASNGGGKQALETVQRLLPVLCQDHGLTPE
QVVAIANNNGGKQALETVQRLLPVLCQAHGLTPDQVVAIANNNGGKQALETVQRLLPVLCQAHGLTPAQVVAIANN
NGGKQALETVQRLLPVLCQDHGLTPDQVVAIASNGGGKQALETVQRLLPVLCQDHGLTPEQVVAIASNGGGKQALET
VQRLLPVLCQAHGLTPDQVVAIANNNGGKQALETVQRLLPVLCQAHGLTPAQVVAIANNNGGKQALETVQRLLPVLC
QDHGLTPDQVVAIANNNGGKQALETVQRLLPVLCQDHGLTPEQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPEQ
VVAIASHDGGRPALE

RH-4
LTPDQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPEQVVAIASNIGGKQALETVQRLLPVLCQAHGLTPDQVVAIA
NNNGGKQALETVQRLLPVLCQAHGLTPAQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPDQVVAIASNIGGKQAL
ETVQRLLPVLCQDHGLTPEQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPDQVVAIASNIGGKQALETVQRLLPVLC
QAHGLTPAQVVAIANNNGGKQALETVQRLLPVLCQDHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPEQ
VVAIASNIGGKQALETVQRLLPVLCQAHGLTPDQVVAIANNNGGKQALETVQRLLPVLCQAHGLTPAQVVAIASHDGG
KQALETVQRLLPVLCQDHGLTPDQVVAIASNGGGKQALETVQRLLPVLCQDHGLTPEQVVAIASNGGGKQALETVQRL
LPVLCQAHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPAQVVAIASHDGGKQALETVQRLLPVLCQDHGL
TPDQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPEQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPEQVVAIAS
HDGGRPALE

RH-5

LTPDQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPEQVVAIANNNGGKQALETVQRLLPVLCQAHGLTPDQVVAIA
SNGGGKQALETVQRLLPVLCQAHGLTPAQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPDQVVAIANNNGGKQAL
ETVQRLLPVLCQDHGLTPEQVVAIANNNGGKQALETVQRLLPVLCQAHGLTPDQVVAIANNNGGKQALETVQRLLPV
LCQAHGLTPAQVVAIASNGGGKQALETVQRLLPVLCQDHGLTPDQVVAIANNNGGKQALETVQRLLPVLCQDHGLTP
EQVVAIASNGGGKQALETVQRLLPVLCQAHGLTPDQVVAIANNNGGKQALETVQRLLPVLCQAHGLTPAQVVAIANN
NGGKQALETVQRLLPVLCQDHGLTPDQVVAIANNNGGKQALETVQRLLPVLCQDHGLTPEQVVAIANNNGGKQALE
TVQRLLPVLCQAHGLTPDQVVAIANNNGGKQALETVQRLLPVLCQAHGLTPAQVVAIASNIGGKQALETVQRLLPVLC
QDHGLTPDQVVAIANNNGGKQALETVQRLLPVLCQDHGLTPEQVVAIANNNGGKQALETVQRLLPVLCQAHGLTPE
QVVAIANNNGGRPALE

RH-6
LTPDQVVAIANNNGGKQALETVQRLLPVLCQDHGLTPEQVVAIANNNGGKQALETVQRLLPVLCQAHGLTPDQVVAI
ANNNGGKQALETVQRLLPVLCQAHGLTPAQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPDQVVAIANNNGGKQA
LETVQRLLPVLCQDHGLTPEQVVAIANNNGGKQALETVQRLLPVLCQAHGLTPDQVVAIANNNGGKQALETVQRLLP
VLCQAHGLTPAQVVAIANNNGGKQALETVQRLLPVLCQDHGLTPDQVVAIANNNGGKQALETVQRLLPVLCQDHGL
TPEQVVAIASNIGGKQALETVQRLLPVLCQAHGLTPDQVVAIANNNGGKQALETVQRLLPVLCQAHGLTPAQVVAIAS
NGGGKQALETVQRLLPVLCQDHGLTPDQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPEQVVAIANNNGGKQALE
TVQRLLPVLCQAHGLTPDQVVAIANNNGGKQALETVQRLLPVLCQAHGLTPAQVVAIASNIGGKQALETVQRLLPVLC
QDHGLTPDQVVAIASNGGGKQALETVQRLLPVLCQDHGLTPEQVVAIANNNGGKQALETVQRLLPVLCQAHGLTPEQ
VVAIANNNGGRPALE

RH-7
LTPDQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPEQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPDQVVAIAS
NIGGKQALETVQRLLPVLCQAHGLTPAQVVAIASNGGGKQALETVQRLLPVLCQDHGLTPDQVVAIANNNGGKQALE
TVQRLLPVLCQDHGLTPEQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPDQVVAIASNIGGKQALETVQRLLPVLCQ
AHGLTPAQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPDQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPEQVV
AIASHDGGKQALETVQRLLPVLCQAHGLTPDQVVAIASNIGGKQALETVQRLLPVLCQAHGLTPAQVVAIASHDGGKQ
ALETVQRLLPVLCQDHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPEQVVAIASHDGGKQALETVQRLLP
VLCQAHGLTPDQVVAIASNIGGKQALETVQRLLPVLCQAHGLTPAQVVAIASHDGGKQALETVQRLLPVLCQDHGLTP
DQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPEQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPEQVVAIASHD
GGRPALE

RH-8
LTPDQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPEQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPDQVVAIAS
NGGGKQALETVQRLLPVLCQAHGLTPAQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPDQVVAIASHDGGKQALE
TVQRLLPVLCQDHGLTPEQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPDQVVAIASHDGGKQALETVQRLLPVLC
QAHGLTPAQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPEQ
VVAIASHDGGKQALETVQRLLPVLCQAHGLTPDQVVAIASNGGGKQALETVQRLLPVLCQAHGLTPAQVVAIASHDG
GKQALETVQRLLPVLCQDHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPEQVVAIASNIGGKQALETVQR
LLPVLCQAHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPAQVVAIASHDGGKQALETVQRLLPVLCQDHG
LTPDQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPEQVVAIASNGGGKQALETVQRLLPVLCQAHGLTPEQVVAIA
SNIGGRPALE

RH-9
LTPDQVVAIANNNGGKQALETVQRLLPVLCQDHGLTPEQVVAIASNGGGKQALETVQRLLPVLCQAHGLTPDQVVAIA
SNGGGKQALETVQRLLPVLCQAHGLTPAQVVAIANNNGGKQALETVQRLLPVLCQDHGLTPDQVVAIANNNGGKQA
LETVQRLLPVLCQDHGLTPEQVVAIASNIGGKQALETVQRLLPVLCQAHGLTPDQVVAIANNNGGKQALETVQRLLPVL
CQAHGLTPAQVVAIASNGGGKQALETVQRLLPVLCQDHGLTPDQVVAIANNNGGKQALETVQRLLPVLCQDHGLTPE

QVVAIANNNGGKQALETVQRLLPVLCQAHGLTPDQVVAIANNNGGKQALETVQRLLPVLCQAHGLTPAQVVAIANN
NGGKQALETVQRLLPVLCQDHGLTPDQVVAIANNNGGKQALETVQRLLPVLCQDHGLTPEQVVAIASHDGGKQALET
VQRLLPVLCQAHGLTPDQVVAIASNIGGKQALETVQRLLPVLCQAHGLTPAQVVAIANNNGGKQALETVQRLLPVLCQ
DHGLTPDQVVAIASNGGGKQALETVQRLLPVLCQDHGLTPEQVVAIASNIGGKQALETVQRLLPVLCQAHGLTPEQVV
AIANNNGGRPALE

RH-10
LTPDQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPEQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPDQVVAIA
SNGGGKQALETVQRLLPVLCQAHGLTPAQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPDQVVAIASHDGGKQALE
TVQRLLPVLCQDHGLTPEQVVAIASNGGGKQALETVQRLLPVLCQAHGLTPDQVVAIANNNGGKQALETVQRLLPVLC
QAHGLTPAQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPEQ
VVAIASHDGGKQALETVQRLLPVLCQAHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPAQVVAIASHDG
GKQALETVQRLLPVLCQDHGLTPDQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPEQVVAIASHDGGKQALETVQR
LLPVLCQAHGLTPDQVVAIASNGGGKQALETVQRLLPVLCQAHGLTPAQVVAIASHDGGKQALETVQRLLPVLCQDHG
LTPDQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPEQVVAIASNIGGKQALETVQRLLPVLCQAHGLTPEQVVAIAS
NIGGRPALE

RH-11
LTPDQVVAIANNNGGKQALETVQRLLPVLCQDHGLTPEQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPDQVVAIA
SHDGGKQALETVQRLLPVLCQAHGLTPAQVVAIASNGGGKQALETVQRLLPVLCQDHGLTPDQVVAIASHDGGKQAL
ETVQRLLPVLCQDHGLTPEQVVAIASNIGGKQALETVQRLLPVLCQAHGLTPDQVVAIANNNGGKQALETVQRLLPVLC
QAHGLTPAQVVAIANNNGGKQALETVQRLLPVLCQDHGLTPDQVVAIANNNGGKQALETVQRLLPVLCQDHGLTPE
QVVAIANNNGGKQALETVQRLLPVLCQAHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPAQVVAIASNG
GGKQALETVQRLLPVLCQDHGLTPDQVVAIASNGGGKQALETVQRLLPVLCQDHGLTPEQVVAIANNNGGKQALETV
QRLLPVLCQAHGLTPDQVVAIANNNGGKQALETVQRLLPVLCQAHGLTPAQVVAIASHDGGKQALETVQRLLPVLCQ
DHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPEQVVAIASNGGGKQALETVQRLLPVLCQAHGLTPEQV
VAIASNGGGRPALE

HB-1
LTPDQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPEQVVAIASNIGGKQALETVQRLLPVLCQAHGLTPDQVVAIAS
NIGGKQALETVQRLLPVLCQAHGLTPAQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPDQVVAIASNGGGKQALET
VQRLLPVLCQDHGLTPEQVVAIASNGGGKQALETVQRLLPVLCQAHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQ
AHGLTPAQVVAIASNGGGKQALETVQRLLPVLCQDHGLTPDQVVAIASNGGGKQALETVQRLLPVLCQDHGLTPEQV
VAIASNIGGKQALETVQRLLPVLCQAHGLTPDQVVAIASNGGGKQALETVQRLLPVLCQAHGLTPAQVVAIASNGGGK
QALETVQRLLPVLCQDHGLTPDQVVAIASNGGGKQALETVQRLLPVLCQDHGLTPEQVVAIANNNGGKQALETVQRL
LPVLCQAHGLTPDQVVAIASNGGGKQALETVQRLLPVLCQAHGLTPAQVVAIANNNGGKQALETVQRLLPVLCQDHG
LTPDQVVAIASNGGGKQALETVQRLLPVLCQDHGLTPEQVVAIASNIGGKQALETVQRLLPVLCQAHGLTPEQVVAIAS
NIGGRPALE

HB-2
LTPDQVVAIASNGGGKQALETVQRLLPVLCQDHGLTPEQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPDQVVAIA
SNGGGKQALETVQRLLPVLCQAHGLTPAQVVAIASNGGGKQALETVQRLLPVLCQDHGLTPDQVVAIASNIGGKQALE
TVQRLLPVLCQDHGLTPEQVVAIASNGGGKQALETVQRLLPVLCQAHGLTPDQVVAIASNGGGKQALETVQRLLPVLC
QAHGLTPAQVVAIASNGGGKQALETVQRLLPVLCQDHGLTPDQVVAIANNNGGKQALETVQRLLPVLCQDHGLTPEQ
VVAIASNGGGKQALETVQRLLPVLCQAHGLTPDQVVAIANNNGGKQALETVQRLLPVLCQAHGLTPAQVVAIASNGG
GKQALETVQRLLPVLCQDHGLTPDQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPEQVVAIASNIGGKQALETVQRL
LPVLCQAHGLTPDQVVAIASNGGGKQALETVQRLLPVLCQAHGLTPAQVVAIASNIGGKQALETVQRLLPVLCQDHGL

TPDQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPEQVVAIANNNGGKQALETVQRLLPVLCQAHGLTPEQVVAIAS
NIGGRPALE

HB-3
LTPDQVVAIANNNGGKQALETVQRLLPVLCQDHGLTPEQVVAIANNNGGKQALETVQRLLPVLCQAHGLTPDQVVAI
ASNIGGKQALETVQRLLPVLCQAHGLTPAQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPDQVVAIASNGGGKQAL
ETVQRLLPVLCQDHGLTPEQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPDQVVAIASNIGGKQALETVQRLLPVLC
QAHGLTPAQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPDQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPEQV
VAIANNNGGKQALETVQRLLPVLCQAHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPAQVVAIASNGGG
KQALETVQRLLPVLCQDHGLTPDQVVAIASNGGGKQALETVQRLLPVLCQDHGLTPEQVVAIANNNGGKQALETVQR
LLPVLCQAHGLTPDQVVAIANNNGGKQALETVQRLLPVLCQAHGLTPAQVVAIASNGGGKQALETVQRLLPVLCQDH
GLTPDQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPEQVVAIASNIGGKQALETVQRLLPVLCQAHGLTPEQVVAIA
NNNGGRPALE

HB-4
LTPDQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPEQVVAIASNGGGKQALETVQRLLPVLCQAHGLTPDQVVAIA
SNGGGKQALETVQRLLPVLCQAHGLTPAQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPDQVVAIASNIGGKQALE
TVQRLLPVLCQDHGLTPEQVVAIASNIGGKQALETVQRLLPVLCQAHGLTPDQVVAIASNGGGKQALETVQRLLPVLCQ
AHGLTPAQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPDQVVAIASNGGGKQALETVQRLLPVLCQDHGLTPEQVV
AIANNNGGKQALETVQRLLPVLCQAHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPAQVVAIASNGGGK
QALETVQRLLPVLCQDHGLTPDQVVAIASNGGGKQALETVQRLLPVLCQDHGLTPEQVVAIASNIGGKQALETVQRLLP
VLCQAHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPAQVVAIASHDGGKQALETVQRLLPVLCQDHGLT
PDQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPEQVVAIASNIGGKQALETVQRLLPVLCQAHGLTPEQVVAIANNN
GGRPALE

HB-5
LTPDQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPEQVVAIASNGGGKQALETVQRLLPVLCQAHGLTPDQVVAIA
NNNGGKQALETVQRLLPVLCQAHGLTPAQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPDQVVAIASNGGGKQAL
ETVQRLLPVLCQDHGLTPEQVVAIASNGGGKQALETVQRLLPVLCQAHGLTPDQVVAIASNIGGKQALETVQRLLPVLC
QAHGLTPAQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPEQ
VVAIASNIGGKQALETVQRLLPVLCQAHGLTPDQVVAIASNIGGKQALETVQRLLPVLCQAHGLTPAQVVAIANNNGG
KQALETVQRLLPVLCQDHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPEQVVAIASNGGGKQALETVQRL
LPVLCQAHGLTPDQVVAIANNNGGKQALETVQRLLPVLCQAHGLTPAQVVAIASNGGGKQALETVQRLLPVLCQDHG
LTPDQVVAIANNNGGKQALETVQRLLPVLCQDHGLTPEQVVAIASNIGGKQALETVQRLLPVLCQAHGLTPEQVVAIAS
NGGGRPALE

HB-6
LTPDQVVAIANNNGGKQALETVQRLLPVLCQDHGLTPEQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPDQVVAIA
SNGGGKQALETVQRLLPVLCQAHGLTPAQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPDQVVAIASHDGGKQALE
TVQRLLPVLCQDHGLTPEQVVAIASNGGGKQALETVQRLLPVLCQAHGLTPDQVVAIASNIGGKQALETVQRLLPVLCQ
AHGLTPAQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPDQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPEQVV
AIASNIGGKQALETVQRLLPVLCQAHGLTPDQVVAIASNIGGKQALETVQRLLPVLCQAHGLTPAQVVAIASHDGGKQA
LETVQRLLPVLCQDHGLTPDQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPEQVVAIASNGGGKQALETVQRLLPVL
CQAHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPAQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPD
QVVAIASNGGGKQALETVQRLLPVLCQDHGLTPEQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPEQVVAIASHDG
GRPALE

HB-7

LTPDQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPEQVVAIASNIGGKQALETVQRLLPVLCQAHGLTPDQVVAIAS
NIGGKQALETVQRLLPVLCQAHGLTPAQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPDQVVAIASHDGGKQALET
VQRLLPVLCQDHGLTPEQVVAIASNIGGKQALETVQRLLPVLCQAHGLTPDQVVAIANNNGGKQALETVQRLLPVLCQ
AHGLTPAQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPEQVV
AIASNIGGKQALETVQRLLPVLCQAHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPAQVVAIASHDGGKQ
ALETVQRLLPVLCQDHGLTPDQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPEQVVAIASNGGGKQALETVQRLLPV
LCQAHGLTPDQVVAIANNNGGKQALETVQRLLPVLCQAHGLTPAQVVAIANNNGGKQALETVQRLLPVLCQDHGLTP
DQVVAIASNGGGKQALETVQRLLPVLCQDHGLTPEQVVAIANNNGGKQALETVQRLLPVLCQAHGLTPEQVVAIASH
DGGRPALE

HB-8
LTPDQVVAIANNNGGKQALETVQRLLPVLCQDHGLTPEQVVAIANNNGGKQALETVQRLLPVLCQAHGLTPDQVVAI
ASNGGGKQALETVQRLLPVLCQAHGLTPAQVVAIANNNGGKQALETVQRLLPVLCQDHGLTPDQVVAIASHDGGKQ
ALETVQRLLPVLCQDHGLTPEQVVAIASNIGGKQALETVQRLLPVLCQAHGLTPDQVVAIASNGGGKQALETVQRLLPV
LCQAHGLTPAQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPDQVVAIASNGGGKQALETVQRLLPVLCQDHGLTP
EQVVAIANNNGGKQALETVQRLLPVLCQAHGLTPDQVVAIASNIGGKQALETVQRLLPVLCQAHGLTPAQVVAIASHD
GGKQALETVQRLLPVLCQDHGLTPDQVVAIASNGGGKQALETVQRLLPVLCQDHGLTPEQVVAIASHDGGKQALETV
QRLLPVLCQAHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPAQVVAIASNGGGKQALETVQRLLPVLCQD
HGLTPDQVVAIANNNGGKQALETVQRLLPVLCQDHGLTPEQVVAIASNIGGKQALETVQRLLPVLCQAHGLTPEQVVA
IANNNGGRPALE

HB-9
LTPDQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPEQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPDQVVAIAS
HDGGKQALETVQRLLPVLCQAHGLTPAQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPDQVVAIASNIGGKQALET
VQRLLPVLCQDHGLTPEQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQ
AHGLTPAQVVAIASNGGGKQALETVQRLLPVLCQDHGLTPDQVVAIANNNGGKQALETVQRLLPVLCQDHGLTPEQV
VAIASHDGGKQALETVQRLLPVLCQAHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPAQVVAIASHDGGK
QALETVQRLLPVLCQDHGLTPDQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPEQVVAIANNNGGKQALETVQRLL
PVLCQAHGLTPDQVVAIANNNGGKQALETVQRLLPVLCQAHGLTPAQVVAIANNNGGKQALETVQRLLPVLCQDHGL
TPDQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPEQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPEQVVAIAS
NGGGRPALE

HB-10
LTPDQVVAIANNNGGKQALETVQRLLPVLCQDHGLTPEQVVAIASNIGGKQALETVQRLLPVLCQAHGLTPDQVVAIA
SNGGGKQALETVQRLLPVLCQAHGLTPAQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPDQVVAIASHDGGKQALE
TVQRLLPVLCQDHGLTPEQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPDQVVAIASNIGGKQALETVQRLLPVLCQ
AHGLTPAQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPEQVV
AIASHDGGKQALETVQRLLPVLCQAHGLTPDQVVAIASNGGGKQALETVQRLLPVLCQAHGLTPAQVVAIANNNGGK
QALETVQRLLPVLCQDHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQDHGLTPEQVVAIASHDGGKQALETVQRLL
PVLCQAHGLTPDQVVAIASHDGGKQALETVQRLLPVLCQAHGLTPAQVVAIASNIGGKQALETVQRLLPVLCQDHGLT
PDQVVAIANNNGGKQALETVQRLLPVLCQDHGLTPEQVVAIANNNGGKQALETVQRLLPVLCQAHGLTPEQVVAIAN
NNGGRPALE

Supplementary Table 1 Primers used in this study. All primers listed 5' to 3'.

See attached Excel file.

Supplementary Table 2 Binding sites of TALEs and Zinc Fingers used in this study. All binding sites listed 5' to 3' (bound N-terminus to C-terminus by TALEs and C-terminus to N-terminus by ZFs).

TALEs

KL-1	TGTGTATGCCCGTGGTG
KL-2	TGGCCCAGCCAGTGTCTG
RH-1	TACACCACTTACCCCTCCCC
RH-2	TTACCCCTCCCCCCCCACAC
RH-3	TATTTGCTGTGGGTTGGGCC
RH-4	TCAGCACAGCAGCTTCCCCC
RH-5	TAGTAGGGTGTGGGGGAGGG
RH-6	TGGGAGGGGGAGTAGGATGG
RH-7	TACATGCAAACACCCACCCC
RH-8	TACTCCCCCCCTCCACCCTA
RH-9	TGTTGGAGTGGGGGCAGTAG
RH-10	TCCTACTGCCCCCACTCCAA
RH-11	TGCCTCAGGGGCTTGGCCTT
HB-1	TCAACTTCTTATTTGTGTAA
HB-2	TTCTTATTTGTGTAATAAGA
HB-3	TGGAATCACAGCTTGGTAAG
HB-4	TCTTCAATATGCTTACCAAG
HB-5	TATGCTTACCAAGCTGTGAT
HB-6	TGCTACTAAAAACATCCTCC
HB-7	TCAAACAGACACCATGGTGC
HB-8	TGGTGCATCTGACTCCTGAG
HB-9	TACCAACCTGCCCAGGGCCT
HB-10	TGATACCAACCTGCCCAGGG

Zinc Fingers

KL-ZF-1	GCTGTCGGTAGGGCGGGC
KL-ZF-2	GCGGAGTCCGCGCGGTGGC
HB-ZF-1	GATGGTATGGGGCCAAGAG
HB-ZF-2	TGTGGGGCAAGGTGAACG
HB-ZF-3	GGTGAACGTGGATGAAGTT
HB-ZF-4	GAGGCCCTGGGCAGGTTGG
HB-ZF-5	GGTGGTGAGGCCCTGGGCA
HB-ZF-6	GAGGCCCTGGGCAGGTTGGT

Supplementary References

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