Supplemental Figure S1. Coding sequence of p16 TALE-DNMT3a-3L.

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Legend:
TALE N-Terminus and C-Terminus
p16 TALE repeat domain
Dnmt3a-3L
2A GFP

Supplemental Figure S2. Jumbled p16 TALE repeat domain.

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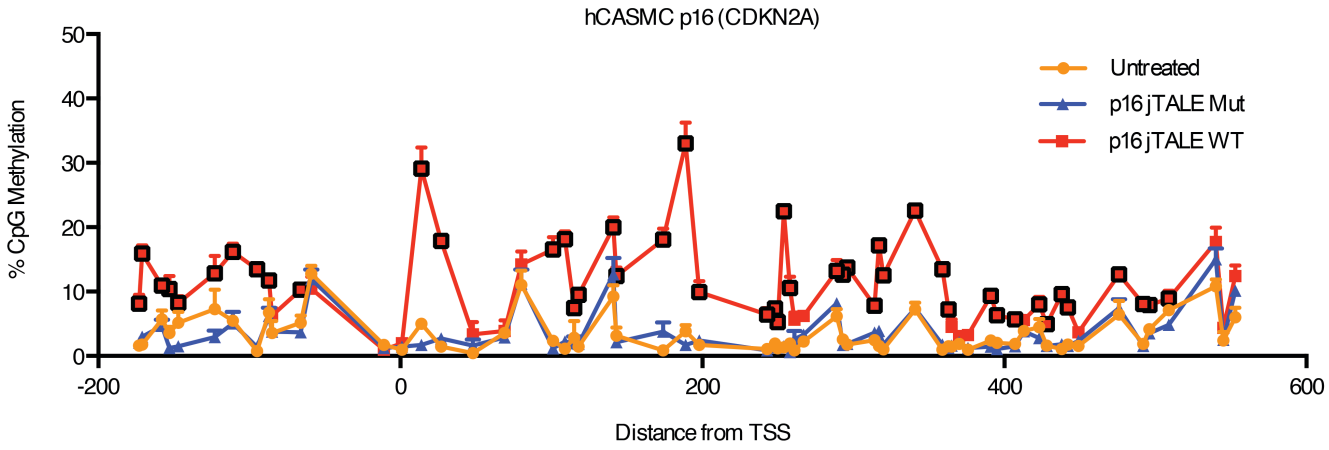
A



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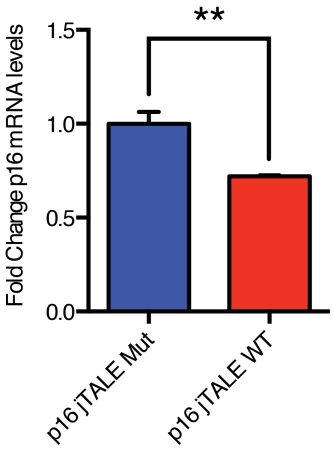
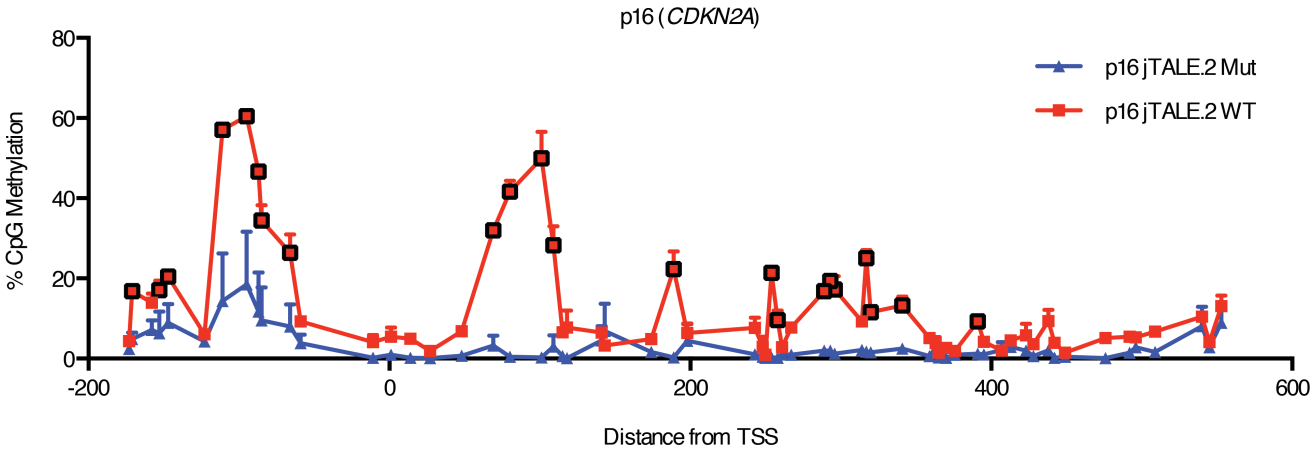


Supplemental Figure S3. p16 TALE-DNMT strategy can be employed in primary human coronary artery smooth muscle cells to decrease p16 expression. Primary human coronary artery smooth muscle cells (hCASMCs) were infected with p16 jTALE-DNMT wild-type or mutant lentivirus. After 4 days of infection, cells were harvested and assessed for DNA methylation **(A)** and p16 (*CDKN2A*) expression **(B)** as described in the main text.

A



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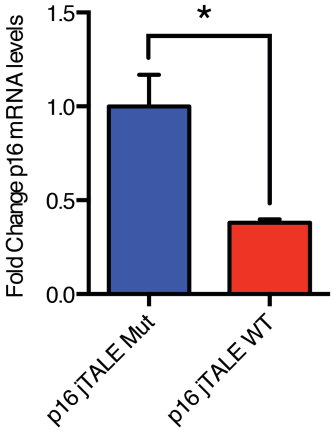

Supplemental Figure S4. Multiple p16 TALE-DNMT constructs can be designed to decrease p16 expression. An additional TALE-DNMT (p16 jTALE-DNMT.2) was designed to target the p16 (CDKN2A) promoter region 118 to 139 base pairs upstream of the transcription start site. Wild-type and mutant infected with p16 jTALE-DNMT.2 were evaluated for DNA methylation **(A)** and p16 (*CDKN2A*) gene expression **(B)** as described in prior human fibroblast experiments.

Supplemental Table 1. **PCR primers for amplification of bisulfite converted genomic DNA.** Primers were designed to PCR amplify regions of interest from bisulfite converted genomic DNA. Each primer pair amplifies an approximately 250-300 base pair region within the CpG island closest to the transcription start site of the gene analyzed. In instances where there was not a CpG island near the gene, the promoter was evaluated. Amplicons were subsequently used to prepare DNA sequencing libraries for DNA methylation analysis.

Locus	Coordinates	Forward (5' to 3')	Reverse (5' to 3')
*CDKN2A*_1	chr9:21,975,075-21,975,330	ATTTGGTAGTTAGGAAGGTTGTA	CCCTAAAATCCCCCCAAATTAAATCTCC
*CDKN2A*_2	chr9:21,974,909-21,975,178	GGTGGGGAGGAGTTTAGT	AACCAACCCCTCCTCTTT
*CDKN2A*_3	chr9:21,974,597-21,974,918	GGGGTTGGTTGGTTATTAGAG	CCTAATTCCAATTCCCCTACAAACTT
*CDKN2A*_4	chr9:21,974,558-21,974,863	AGAGGGGGAGAGTAGGTA	CCAAAAAACCTCCCCTTTTTCC
CDKN2A_CGI2	chr9:21,970,930-21,971,229	GTATGGTTATTGTTTTTGGTGTTT	ACCATTCTATTCTCTCTAACAAATCA
CDKN2A_CGI3	chr9:21,968,280-21,968,569	AGGTTAAAGATGTGTGGTATATT	ACAACCACTAAAACTCATTATATAAC
CDKN2A_CGI3_2	chr9:21,968,551-21,968,805	AATGAGTTTTAGTGGTTGTTTATAAT	AACACATAAATAAATAAACATCCATT
ACTB	chr7:5,570,376-5,570,636	TGGGAGTTTAGTGTTTAAGAGATGTTTA	CCCTCTCCCCTCCTTTTAC
*CDKN2B*_1	chr9:22,009,012-22,009,290	AGGAGGGGTAGTGAGGATT	ACACTCTTCCCTTCTTTCC
CDKN2B_2	chr9:22,008,863-22,009,088	GGGTAATGAAGTTGAGTTTAGG	CACCTTCTCCACTAATCCC
p14ARF	chr9:21,995,629-21,995,928	TGGGAATAGTAAAAGTAGGGTAAGG	ACACCCACCCACTCAAAC
MTAP	chr9:21,802,505-21,802,762	GGAAAGGTTTGTAAAAGGG	AATACCAAAAACCATATCTACAC
IFNE	chr9:21,481,642-21,481,862	GAAAAGGGAATTTGAAAATTTAATGT	AATAAAAACCAACAACACCAACACA
CDKN2C	chr1:51,435,514-51,435,751	GGAGGATTTGTTTTTGTAGTTTTG	CACAAACACACATACATTCCTAATT
CDKN2D	chr19:10,679,809-10,680,058	TTTATAGGGTTTGTATAATTAGTGG	CTACCTCCCTTCCCTCAAA
CDKN1A	chr6:36,651,742-36,651,971	GATTAGTTGGAAGGAGTGAGAGA	ACTCAACTACTCCCTATCCACTAAAC
CDKN1B	chr12:12,869,846-12,870,092	GGGTAGAGTTGGGGGTAG	ACAAACCTACTCTAACTAACCT
CDKN1C	chr11:2,907,681-2,907,919	GGTTTGGTTTAAGGTTGAGAAG	AACCCTCACACACCTACT
RB1	chr13:48,877,360-48,877,609	GTGATTTTAAAAGGTTAGTAAGTG	AAACCTCATCCCTATCCC
CDK4	chr12:58,145,866-58,146,110	GGTGAGGGGGTTTTTTTAGT	ACCCTTCCATAACCAACTC
CDK6	chr7:92,462,912-92,463,146	GGTTTGGGAGAGGGTAGG	ATCCCTCCTCTTCCCTCC
CCND1	chr11:69,455,880-69,456,104	ATTATAGGGGAGTTTTGTTGAAGTT	CAACACAAAAACTAATATTCCATAAC

Supplemental Table 2. qPCR primers for gene expression analysis

Locus	Forward (5' to 3')	Reverse (5' to 3')
HPRT1	GCAGACTTTGCTTTCCTTGG	AACACTTCGTGGGGTCCTTT
CDKN2A (p16)	CCCAACGCACCGAATAGTT	AGCAGCAGCTCCGCCACT
CDKN2A (p14ARF)	AGAACATGGTGCGCAGGT	GGGATGTGAACCACGAAAAC
CDKN2B	GCTGTTTCATCAGCAGCCTA	CCACAATGGAGCTAGAAGCA
MTAP	CTACCTCAGGGCATGGTTGT	TGCTGGCTAAATGCTTGTTG
IFNE	ACCCTTGAACGACATGAAGC	AAGAATCATGTCTGGAGAAGTCC
CDKN2C	GTGATTTGGCCAGGCTCTAT	AGCCCTCCCCACGTTTATT
CDKN2D	CCAAGGGCAGAGCATTTAAG	AAGCAACGTGCACACTTCAG
CDKN1A	GATTAGCAGCGGAACAAGGA	CAACTACTCCCAGCCCCATA
CDKN1B	GAGGTGCTTGGGAGTTTTGA	TGTTTACACAGCCCGAAGTG
CDKN1C	CAGCGTTCGGTTTTGTTTTT	GGGACCAGTGTACCTTCTCG
RB1	AGGGCTTACTATTTCTGGGTCTT	CAATACACGATCTCTGAAGTTCC
CDK4	CGAGCTCTGCAGCACTCTTA	AGAAGGGAAATGGCAGCTTT
CDK6	TGTCTATCTCCCGGCACTTC	TGAAAGCAAGCAAACAGGTG
CCND1	AGCGCTGTTTTTGTTGTGTG	CTTGCCTCAAAGTCCTGCTT