a

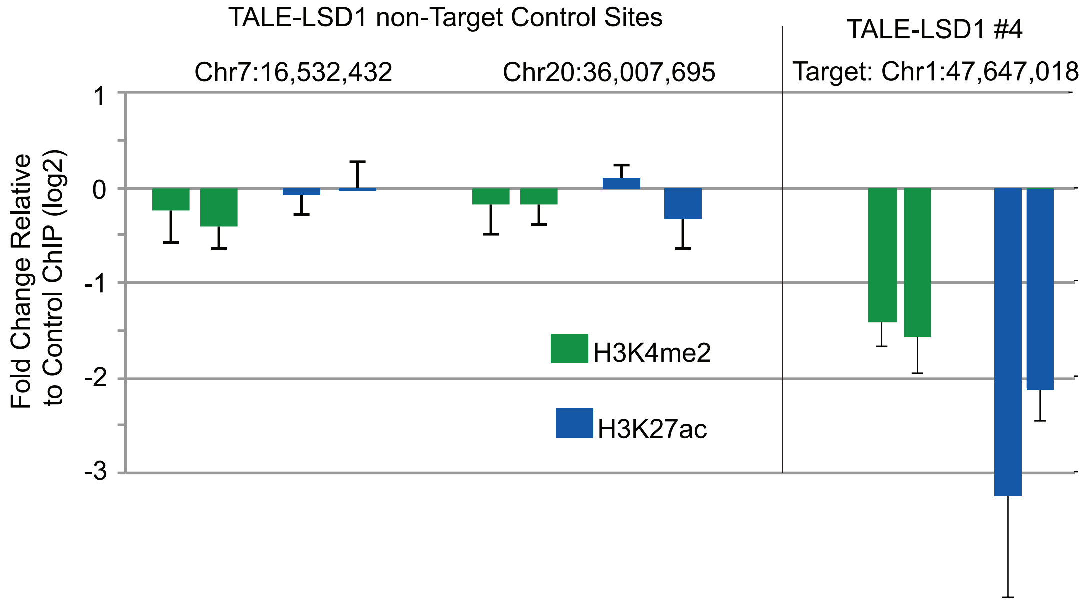
TALE-3X Flag ChIP-seq Peaks

chr location	Rep1 tags	Rep2 tags	pvalue
chr1:47,646,591-47,647,590	25	20	0.01
chr1:17,221,975-17,222,974	3	8	0.14
chr5:78,850,956-78,851,955	5	1	0.21
chr17:51,183,234-51,184,233	2	4	0.15

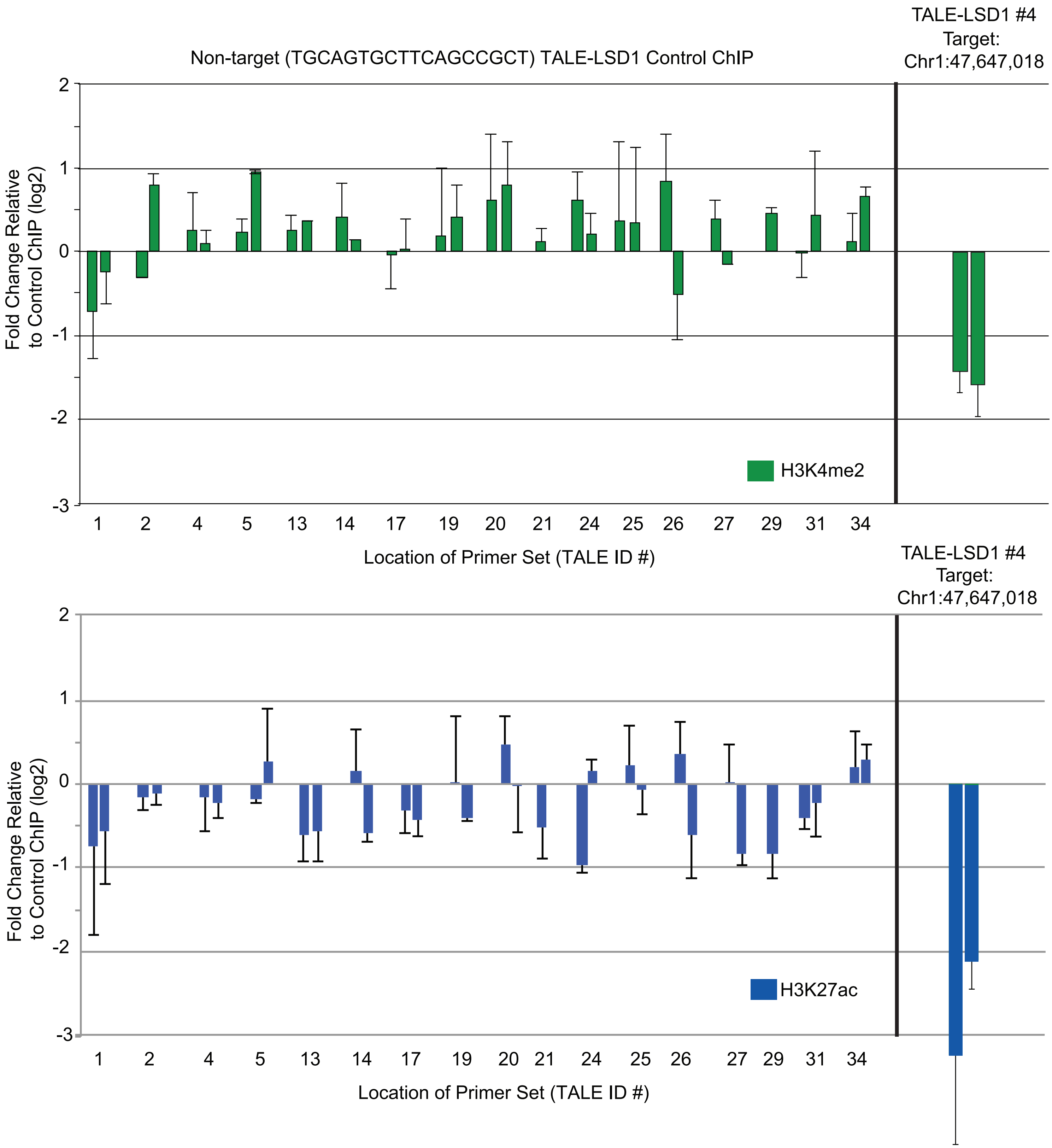
b

Target Sequence	TALE-3X Flag ChIP tags per 1kb bin	Input tags per 1 kb bin
18/18 Target (n=1)	17.5	1
17/18 Targets (n=2)	0.5	0.5
16/18 Targets (n=52)	0.40	0.58

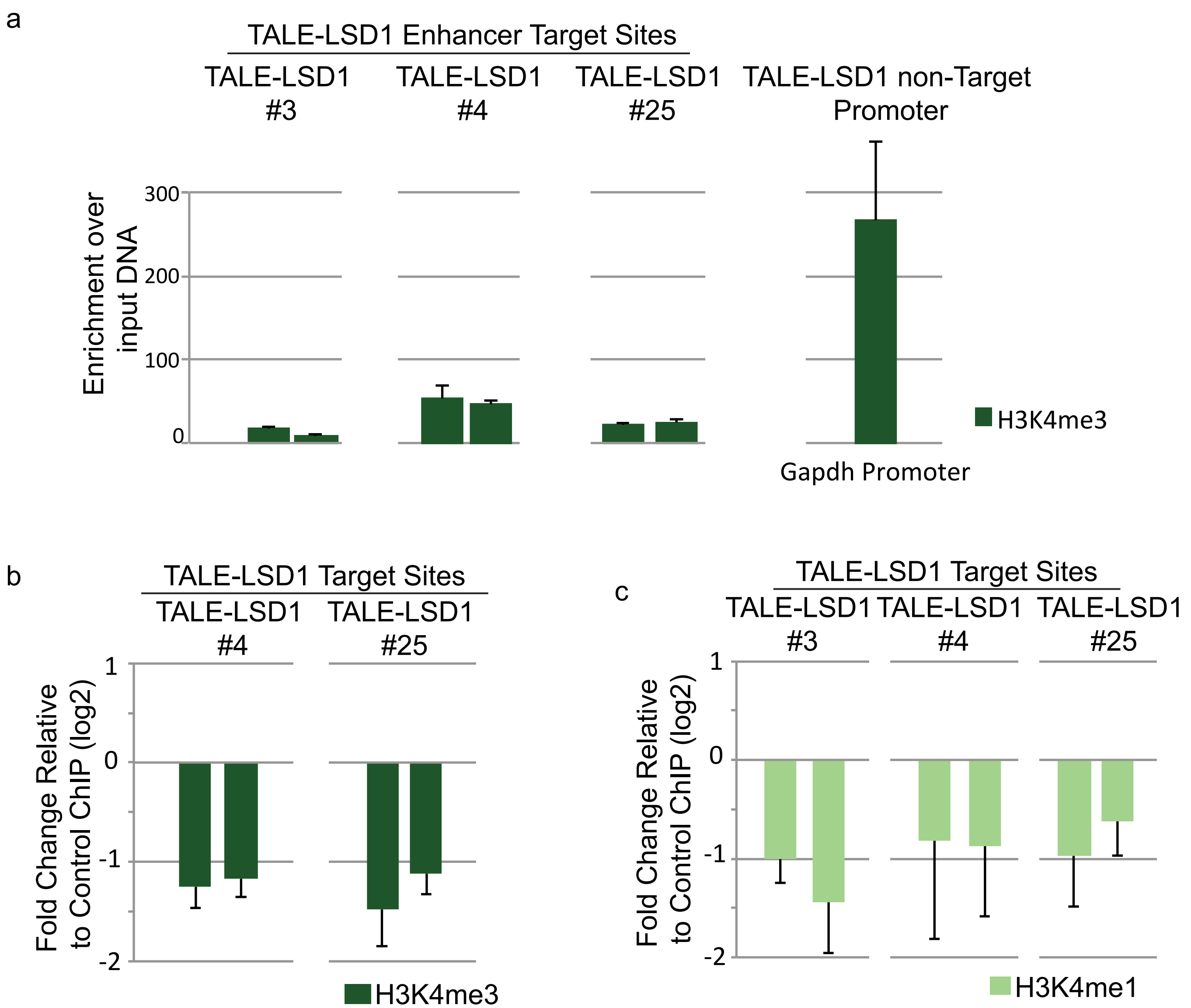
Supplementary Figure 1. Specificity of TALE binding determined by TALE-3X Flag ChIP-seq.
(a) Peak calls using MACS in two biologically independent replicates along with reads falling within a 1 kb window around the peak. Yellow shade indicates the target locus. P-values calculated by comparison of both biological replicates to the input control library.
(b) The sequence read count at 54 genomic loci with 1 or 2 mismatches compared to the perfect match target locus for the TALE-3X Flag.



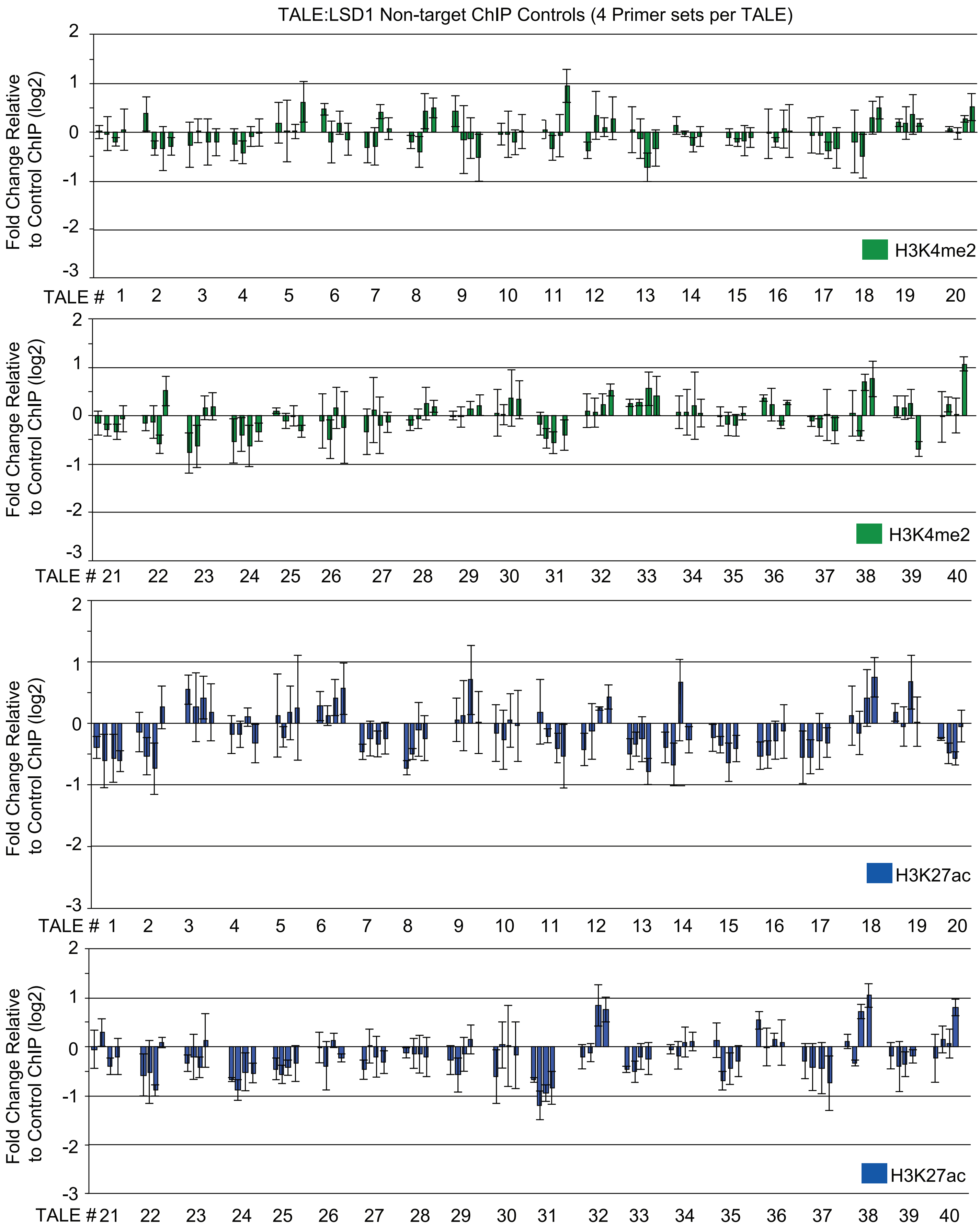
Supplementary Figure 2. ChIP-qPCR to test for off target effects of TALE-LSD1.
ChIP-qPCR for H3K4me2 (green) and H3K27ac (blue) at two non-target control enhancers. For comparision, the data from the target enhancer is shown.



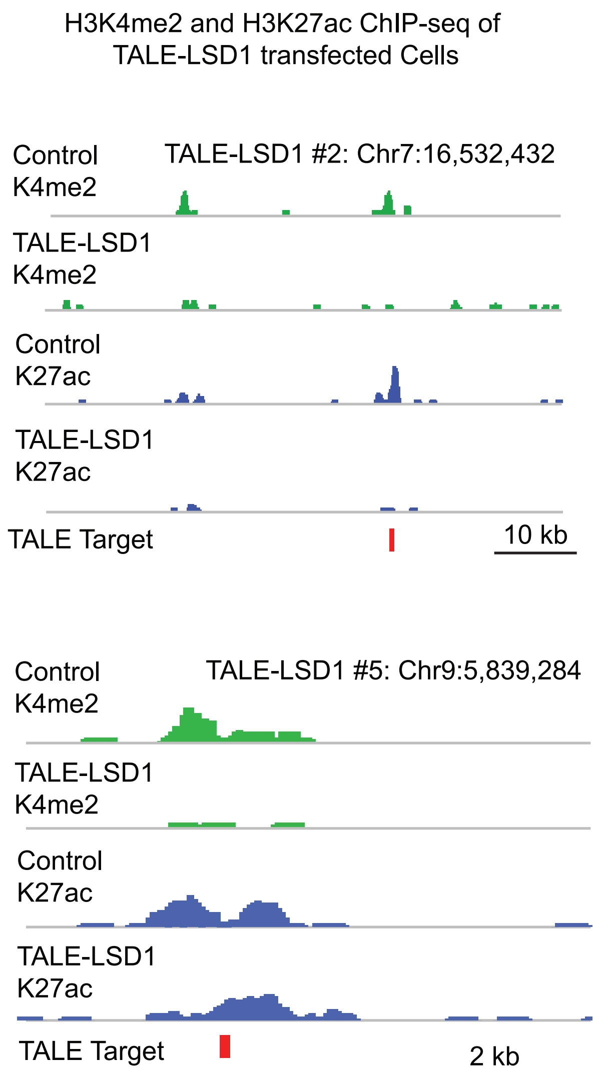
Supplementary Figure 3. ChIP-qPCR values for the non-target control TALE-LSD1.
A TALE-LSD1 construct targeting a sequence not present in the human genome was transfected into K562 cells as a control for non-specific effects. Data is shown as ratio of enrichment to mCherry plasmid control for a subset of enhancers shown in figure 2. For comparision, an 'on target' TALE-LSD1 construct at it's targeted enhancer is shown (TALE-LSD1 #4).



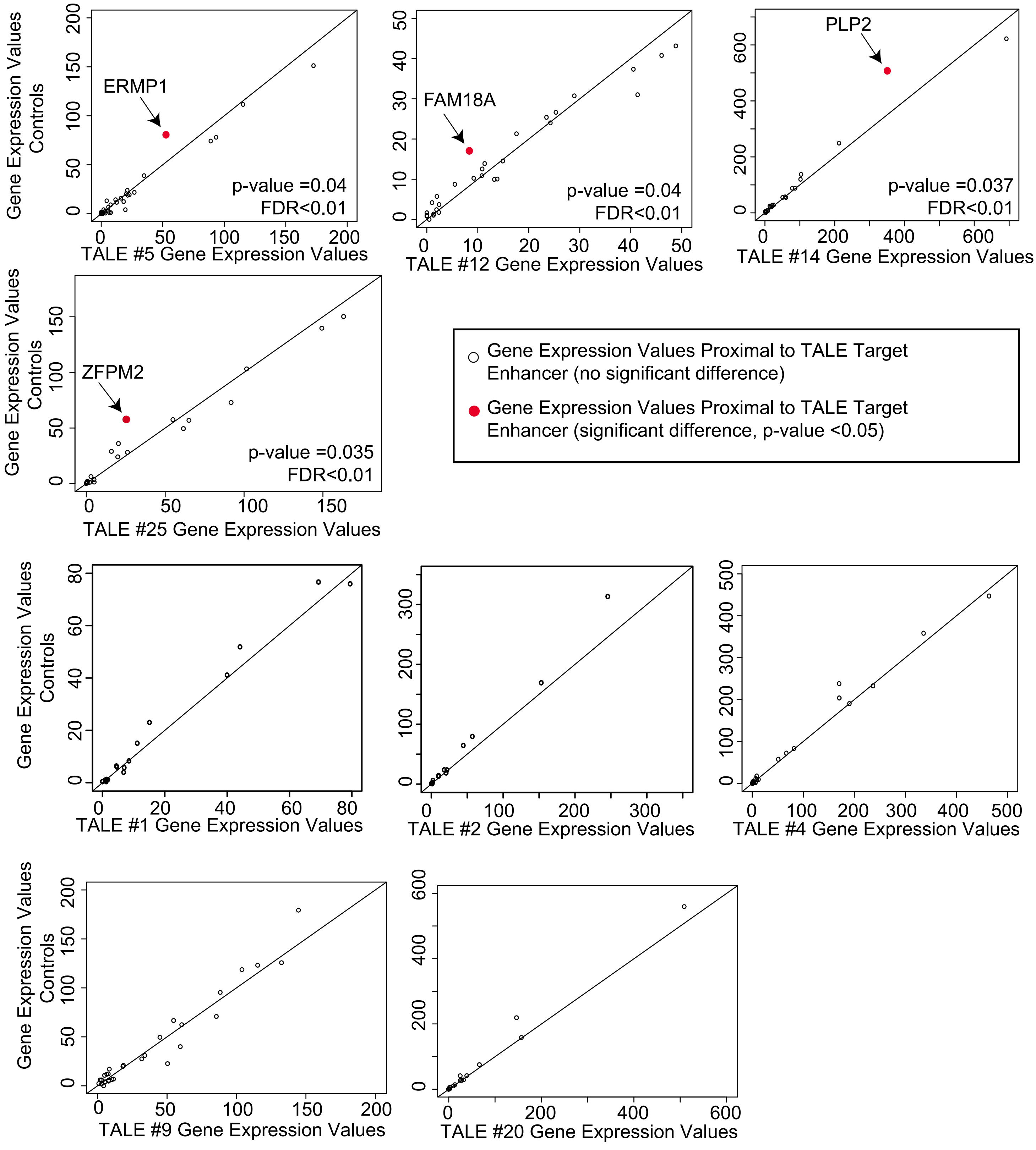
Supplementary Figure 4. ChIP-qPCR to test for effects of TALE-LSD1.
(a) ChIP-qPCR enrichment of H3K4me3 for three target enhancers, selected based on prior evidence of H4K4me3 (#4, #25) and one typical enhancer (#3) lacking K4me3. For comparision, data from a H3K4me3 enriched promoter is shown.
(b) ChIP-qPCR for H3K4me3 (dark green) at the two TALE-LSD1 targeted enhancers that showed some H3K4me3 enrichment. The data represent the decrease in enrichment at the target enhancer.
(c) ChIP-qPCR enrichment of H3K4me1 for target enhancers of three TALE-LSD1 fusions. The data represent the decrease in enrichment at the target enhancer.



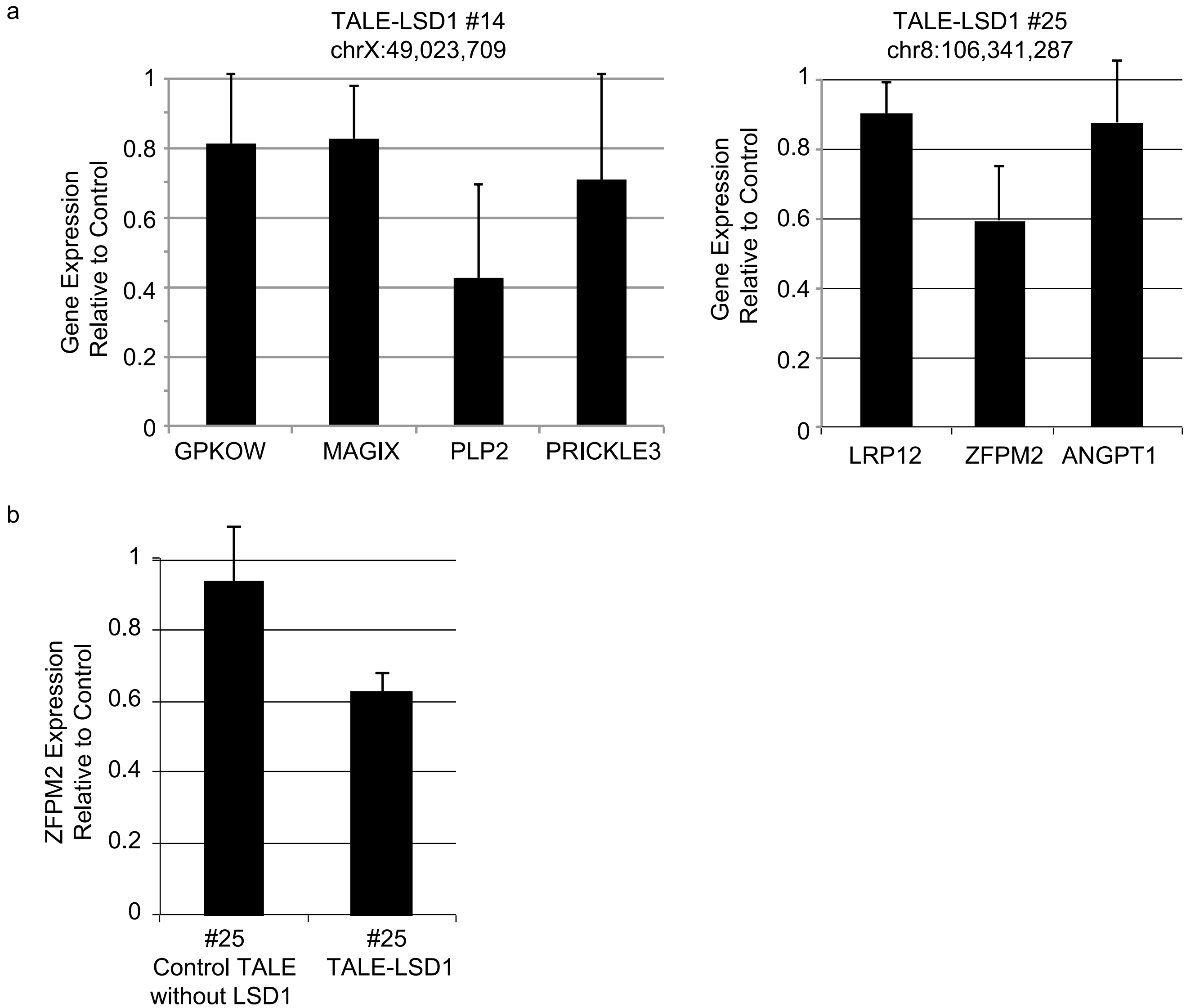
Supplementary Figure 5. ChIP-qPCR for H3K4me2 and H3K27ac at non-target sites. Data is shown for all 40 TALE-LSD1 constructs used in Figure 2. Four primers sets were used to measure ChIP enrichment at two non-target enhancer loci for each TALE construct. No non-target enhancer showed a significant decrease (>2 fold decrease in 2/4 primer sets) in ChIP enrichment.



Supplementary Figure 6. ChIP-seq maps for H3K4me2 and H3K27ac for control cells and cells transfected independently with 2 TALE-LSD1 fusions.



Supplementary Figure 7. Mean normalized 3' Digital Gene Expression Values for the 10-25 genes nearest the TALE target enhancer. Genes with values below 10 were considered unexpressed in K562 cells. Red data points represent genes with a significant decrease in the TALE-LSD1 transfected cells. Significant decrease was considered if both biological replicates represented the two outlying values across all 22 RNA-seq datasets (see Methods).



Supplementary Figure 8. Quantatitative PCR confirmation of 3' DGE. (a) RT-qPCR expression analysis for genes near two TALE-LSD1 target sites.
(b) RT-qPCR data showing gene expression for Zfpm2 in cells transfected with a TALE #25 control plasmid that lacks the LSD1 protein, with data from the TALE-LSD1 for comparision. Error bars represent +SEM, n=2 biological replicates.

Supplementary Table 1. TALE Array Target Sequences

TALE ID#	chr #	TALE Target Sequence
1	chr12:25,845,475	TTCAGTTGTGGTATCTG
2	chr7:16,532,432	TACCATGTCTTTCTAAG
3	chr3:141,765,325	TTTACAGAGCTGTGGTCACT
4	chr1:47,647,018	TCCGTGGCTGCCAGTCTG
5	chr9:5,839,284	TGCATATACTTTTTAATG
6	chr1:47,646,996	TCCAGGAGCGCGCCTGAG
7	chr7:129,598,655	TGCCTGTGAGGAACAGCTGT
8	chr2:169,708,409	TGCAGACATCTCCAGGCTCT
9	chr9:102,832,599	TAATTTGTACATGGTTACAT
10	chr15:38,894,009	TGTTAGTTACCATATTGTGG
11	chr8:106,347,824	TCCAGTCCCTGGCTCCCATG
12	chr16:10,832,743	TGGCTAATTTTTGGTATTTT
13	chr4:145,245,496	TGGCTTTCCTTCCCTTTG
14	chrX:49,023,709	TAGCCGCGAGGAAGGCG
15	chr5:162,806,718	TAAAGACCTGTTACCCAATT
16	chr4:145,050,452	TCGTTTTTCTTTTTTGGAAG
17	chr7:129,515,859	TTCTAAATTGAGGTGCTG
18	chr10:11,183,638	TCAATCATTGCATGTTTATT
19	chr17:8,323,819	TTGCATCTGGGACAGATG
20	chr11:5,245,852	TTGATGGTAACACTATG
21	chr1:182,269,308	TTATCTCCCTCACCCAG
22	chr1:198,568,183	TGGTTAGAAACACAGCTGCC
23	chr6:138,240,975	TTCATGGTTCAATAAAGACT
24	chr3:150,169,053	TACATAAAATTTTTAAGG
25	chr8:106,341,287	TTAAGCTTCTGAAGTCAG
26	chrX:119,619,445	TGATCTTCATTTTTAAAG
27	chr21:15,825,632	TGGTATGAGTTGAAAATG

28	chr8:106,376,850	TAAGTCTACATATAGTATCC
29	chr11:16,617,852	TAAAATGCACTCACAATG
30	chr19:14,496,304	TCTCTGAATCCCCTGGTGAC
31	chr6:119,634,206	TTAAACAGATAAGGGAG
32	chr1:47,646,977	TGGTGCGTTATCAGCCTT
33	chr8:106,256,324	TCAATACCCCACAAAGAAGC
34	chr20:36,007,695	TCTCTACCTTGGAGGCTG
35	chr1:166,674,281	TAGAAAATACAACCTCAG
36	chr11:48,082,936	TCCTGGAAAAGCCCTCTATG
37	chr14:23,030,549	TAAGTTTGCAAACAAGCTCC
38	chr19:23,907,083	TGGCTTTCCTAGGCAGAAGT
39	chr10:80,948,325	TCACGCCTTTGTGGCCAGAG
40	chr18:32,630,094	TCACTGTGTACCTTTTTATG
non-Target	N/A	TGCAGTGCTTCAGCCGCT

Supplementary Table 1 **Primer Sequences Used**

TALE ID #	ChIP qPCR Primer Set	F	R
1	1.1	GGAATCGTGAATACCCCTGA	AACATGCAGGTCTGCTTTCC
1	1.2	GGAATTGGCCTGCAGAATTA	GTACACCATTGGCTGGCTCT
2	2.1	TACTGACCCATGAGCACAGC	CCCCACTGCCATCCTACTTA
2	2.2	GAGTGTTGGCAGAATGAGCA	TGTGCGTATGCATTTTGTTCT
3	3.1	AGCACACAATTTTGCTCATCA	ACGTGCACATGGAACAAGAC
3	3.2	CTGCCAAGTTTCTGGTTGGT	GAGACAAAATAGCGGGGACA
4	4.1	AAGAGGACATTCTGGGCTGA	CCTGCCTCCTAAGCTTCCTT
4	4.2	GACCTGACTCGAACCCACTC	GCCTCTGCTAAGGCACAAAC
5	5.1	TGCCTAGGAAGGCACTTGTC	GGCTGGAGATCAGCTTTTTG
5	5.1	TGTCCTGGAACGGTTTCACT	TTTCTCCTTTGGGCATCTTG
6	6.1	AAGAGGACATTCTGGGCTGA	CCTGCCTCCTAAGCTTCCTT
6	6.2	GACCTGACTCGAACCCACTC	GCCTCTGCTAAGGCACAAAC
7	7.1	CCCTTGACCAGGTAGGTTCA	AAGGAGGGCTCCAGTTTCAT
7	7.2	TGGTGGAATGAGTAGCAGAGC	GGGGATTTTCACACTTGGTG
8	8.1	TGTCTGCACAAATTGCTGTG	CTTGGGAGGGGTTCAGAGAC
8	8.2	ACTCAAAGGTGGGTGTGAGG	TCCGATAATCTGGTCCAAGG
9	9.1	CCCAGGAAACTTGATGAGAGA	TGTGGAAGGAGTGAGTGAACA
9	9.2	GGGTTTTCATGAAGCTTTGAA	TTTCGTATTGCATCCCATCA
10	10.1	GCTGAGCTTTTCAGGTAGGC	GCTCCCAAAAAGATGCAAGT
10	10.2	GGGCCCTCCTTATACTTGGA	TGGACTGGGAGGAACATAGC
11	11.1	TGCTACGTGCAGCGTATTCT	TGCAACGCTATTTCTCAGGA
11	11.2	AGCATTTTCAGCCTCAGTGG	CCTTGTAGCACCTCTGTCCA
12	12.1	CAGACTTCTGGAACGCAGTG	TGTGACAGGCCAAGTCTCAG
12	12.2	CTGACGGTTTATGAGCAGCA	GTTTCCCACAGTTCCCTGAA
13	13.1	TGAAGTCCACATGTTTAGCTCCT	TGGAAGGAATGTGATTCCACT
13	13.2	TTCAACAGCAACCAGGAATG	AAGCTCAAAAAGAAAAACTTCAACA
14	14.1	CCATTTTCCGTACATGGTGA	CTGGCTGTAGGGCTCTGTTC
14	14.2	GACGGGGAAGGAAGAAAGAA	TCCCAGCTCTCGCAGCTT
15	15.1	TACACAACAGCACCCACACA	CCCCATTTCAGTTCTTTCTCA

15	15.2	TCTTCTGGGTTTGTTGGCTA	GGCACCATGTGAACTCTCCT
16	16.1	TCCAACTCAATGCCTTTTCTG	CACAGGCAAGATTCCCATTT
16	16.2	AATGGCTCTGGAGAAAAGCA	GCATGCCAGTCTGAAGATGA
17	17.1	TGTGAACCTCGAGAAGTGTGA	TTGTTGAGGTGTGCATGAGG
17	17.2	GTCATGTCCAGCAGGATGC	ATGCAGCTGACCCATTGTTT
18	18.1	ACGATGGAGGACATTGGAAG	TGAAGGCTTTTCAGGAGCTT
18	18.2	CTGCAAACAAGGTCTTTGGAC	AGGCAGCTACCTGGTTAAGG
19	19.1	GTGACCTTGGAGACGTTGCT	AGCCTCTTGAACCAGAGCAG
19	19.2	AAGAGAAGGAGAACCAAGCCTTA	CACACCAGCAAAGAGCAAAA
20	20.1	GATTCCGGGTCACTGTGAGT	TTTTACGGCGAGATGGTTTC
21	21.1	GGAAGAAAGGAAGGTAGGAAGG	AGGGCACTCTCCTCTCCTCT
21	21.2	GCTGAGACCACCCACTCTTC	CCCAGAAGGAATTACCCACA
22	22.1	TCACACATCACTTGCGTTCA	TGGCTTGATAACCCAACCAT
22	22.2	AGGGAGCACTCTAGGGATGG	CAGGGGAAACAGGAAGTGAG
23	23.1	CCACTAAACCGCAACCAAAG	GGAAACTCCCAGCTTTCAAAC
23	23.2	CGTTTCTCCCTGGGTTCTTT	ATTTTTCTGCCTCCCAAACC
24	24.1	CTGCCCCCAAAGAAAGGTAT	TTGGCATACTTCATGCTCACA
24	24.2	TTGACATTAGGTCCAGGTTTGA	TATTTTAGGGCAGGCACACC
25	25.1	TCATTTTGGTAGCCTTTCTGC	CACTCAAGTCCCAGGTTGGT
25	25.2	GATGATTTGGCTTTTGCGATA	CTTGTGGGAGCTCGACATTA
26	26.1	GACGTGTTGGTGCATACCTG	ATGAGGCTCCTCCCTCATTT
26	26.2	TCAAGAGTACGGCAATCACG	GGGAAACCGAAGGATTGATT
27	27.1	GACCACCGGTCTTCTCATGT	GCAGCTGATGAAGAGCAGAA
27	27.2	TAGGGTGTGGATGTGGAACA	TGGGAAATTGCTGTGTTGAG
28	28.1	TCCTGTAAAGTCCTCAGATCAACA	GCCAGCTTCTAAGGATGCAC
28	28.2	TTGGTCTTTGGCCTTCTAGG	AATGGGGAAGTGACAAGGAA
29	29.1	CAGCCTTTCTAGGAATCACAAA	GGATGATGAGGAACTGGCTTT
30	30.1	GTGAACCACCAAGCACAGC	AGCAGGGGTGGAGAGAAAAT
30	30.2	GGCTACAGCGTCTTCCTGTG	CACACACCACACCCACAACT
31	31.1	TAAGGCCGGTCTATCACAGC	GCAGTCTCAGCACCTCAACC
31	31.2	ACTGCCTGCCTGGAGTCTAC	TCGCTCACTGAGGAATGATG

32		32.1	TACACCGCGAAGGATAGTC	TGGGGGTCAGAGAGAGAATG
33		33.1	GGGCCCCAGACTTTAATTTG	GCCTCTGGAGTGCAGTACCT
33		33.2	CCCAGATATTTCCTGCTCCA	CCCCCAAATTCCATTATTCC
34		34.1	GAGGGAGCGAGCCATAGTG	ACAATGGGGCTGCCTGAG
34		34.2	GGAGGAGGGTGGTCTCTCAT	TCGAAAGCTACACGGCTCTT
35		35.1	TGGGTGAGGAAGGAGAAAGA	AAACCCCTATGGGCAACTCT
36		36.1	CTGGCCCTCTTCTCCTTTCT	CAATCATTTGCCAACACAGG
36		36.2	GTCTGAGGAAAGGCACCTGA	TCGCACCTGTGTGAGAGGTA
37		37.1	AGCGACAAAAGGTCAACAGA	GGTGTTGCGGAAAACACTTT
37		37.2	CCTAAGAATCAGAAACGCAATG	CAGTCTGGGCAACAGAACAA
38		38.1	AACGAAACACAACCTGCACA	CTGTAACCCTACCCCCAACC
38		38.2	CAGAACAAAATGGAGTCTTAGCC	TCAGAAGGTGTGGGGAAAAG
39		39.1	ATGGCTTTCATGAAGCTGGA	CGTCTGTGCGAAGAGAAGC
39		39.2	AAAGCATTTTTGCCATCCAG	TTCCCGGTTAGATGAGTTGG
40		40.1	GCCCTCCCTTGATAAGAACC	TGGGAACCTCTCCATCTCAC
40		40.1	CCAAAGTCACATGGATGACAG	GGCTAAATGAGGCAGATGCT
N/A	BC.1		CCTAGGCAACAGTGACACCTATTT	AAAAATCAGTTTGTGTGTTTGTGG
N/A	Gapdh Promoter		GAAGGTGAAGGTCGGAGTCA	CCCATACGACTGCAAAGACC
TALE ID #	cDNA qPCR Primer Set		F	R
#14	GPKOW		CTGAGGGAAGACATGCTGGA	AGTGAAGCTCCACCACCTGA
	MAGIX		CCCAGCTCCACCTGGTTATT	CTAGGGAAGTGCTGCTGCTG
	PLP2		ATGTGTGACCTGCACACCAA	CTTTACCCCTGCGACGATTT
	PRICKLE3		GGCACCAGCACAGAGTTAGC	GACGACCGAAGGCACTATCA
#25	LRP12		GAAGCTCCTCCCTCGTATGG	TCCAAGCTGAGATCGTACCG
	ZFPM2.1		ATCAGATTTCCAGCCTGTGC	TGATCACGGAATCAGCAGTG
	ANGPT1		CTGGGACAGCAGGAAAACAG	TAGATTGGAGGGGCCACAAG
	ZFPM2.2		GGCCTGAAAATCTGAGCTGC	CAGTCGTCTGTCTCAACTCCA
	ZFPM2.3		GTACAGCAAAGGGGGTCAGC	GACTGGCAGCTTGTAGCCTT
	ZFPM2.4		GTTTTATCTTTTGAAAGGCACAGTC	TTGTGATCACCAGGTGCAGT
	ZFPM2.5		TCAATTCAGCTGCTTCCTCA	CTGGAAATCTGATGGGCACT

SDHA	TCTGCACTCTGGGGAAGAAG	CAAGAATGAAGCAAGGGACA
TBP	TTCCCCATGAACCACAGTTT	TGCAATACTGGAGAGGTGGA