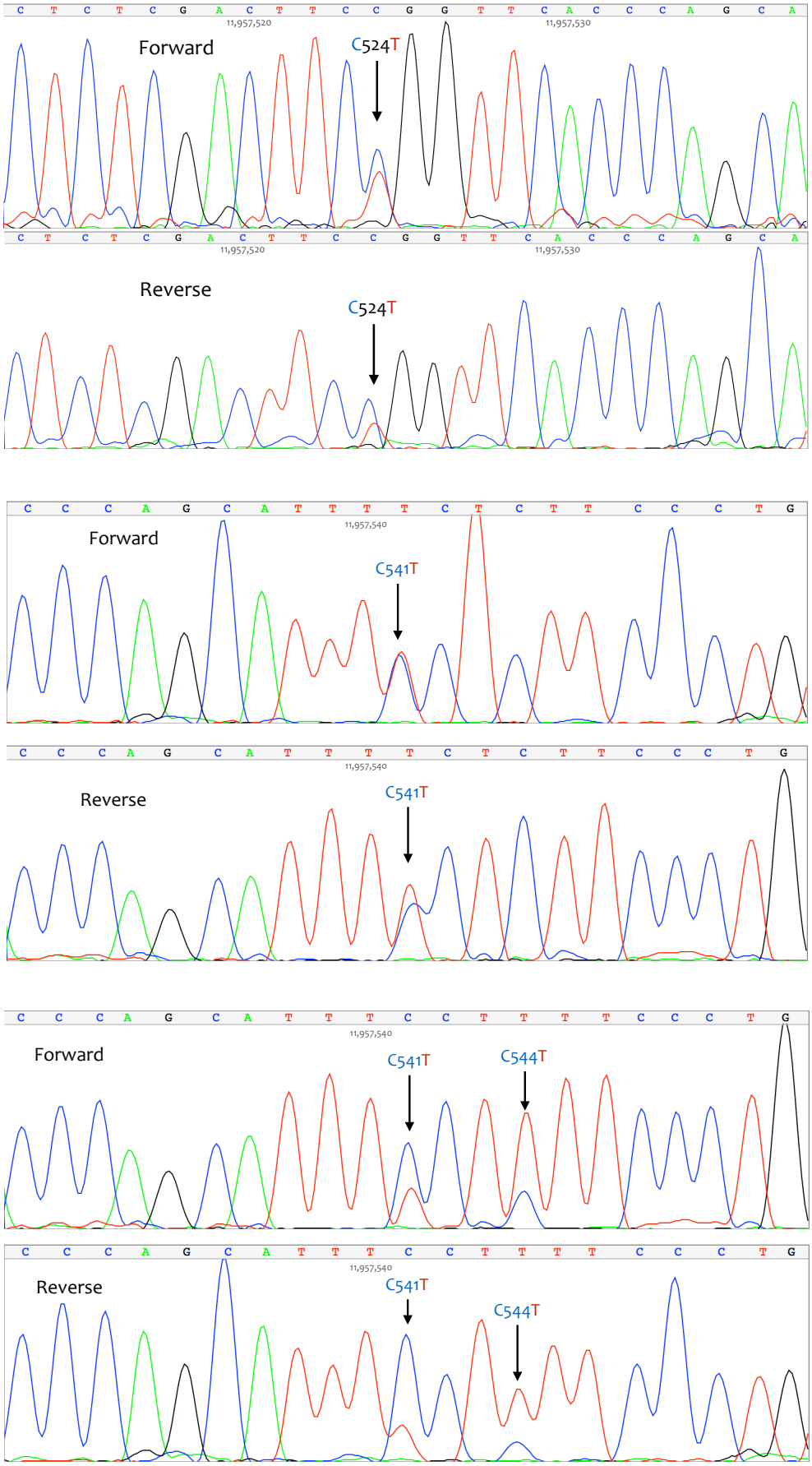
SUPPLEMENTARY FIGURES AND TABLES

Tongwu Zhang *et al.*

SDHD promoter mutations ablate GABP transcription factor binding in melanoma

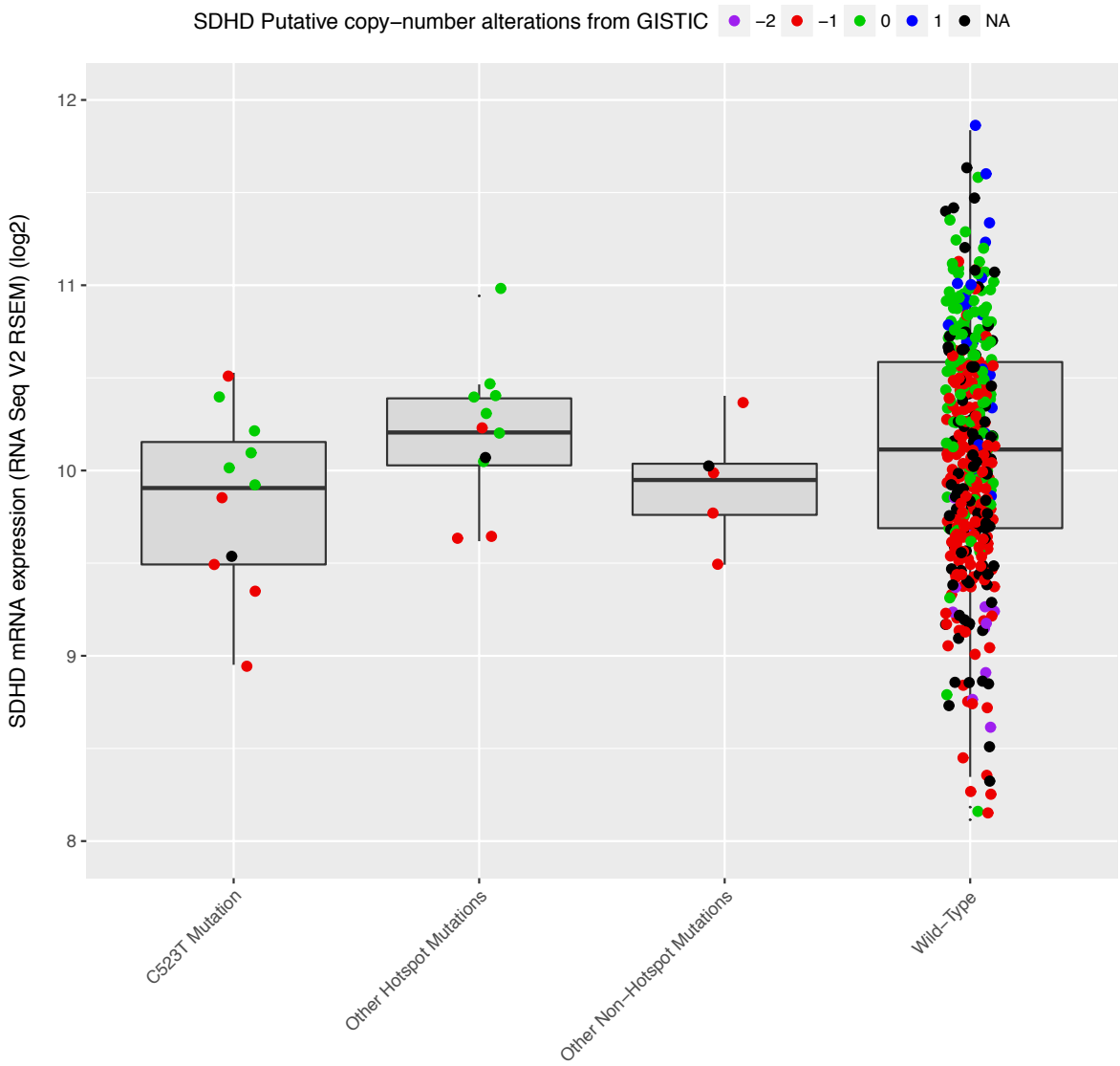
Supplementary Figure 1. Confirmation of the recurrent C524, C541 and C544 *SDHD* promoter mutations in melanoma cell lines. Sanger sequencing traces for both forward and reverse reads verify all three recurrent *SDHD* promoter mutation in melanoma cell lines UACC952, C021 and C077.

Fig S1


UACC952
Forward
C524T
11,957,520
11,957,530
Reverse
C524T
C021
Forward
C541T
11,957,540
Reverse
C541T
C077
Forward
C541T
C544T
Reverse
C541T
C544T

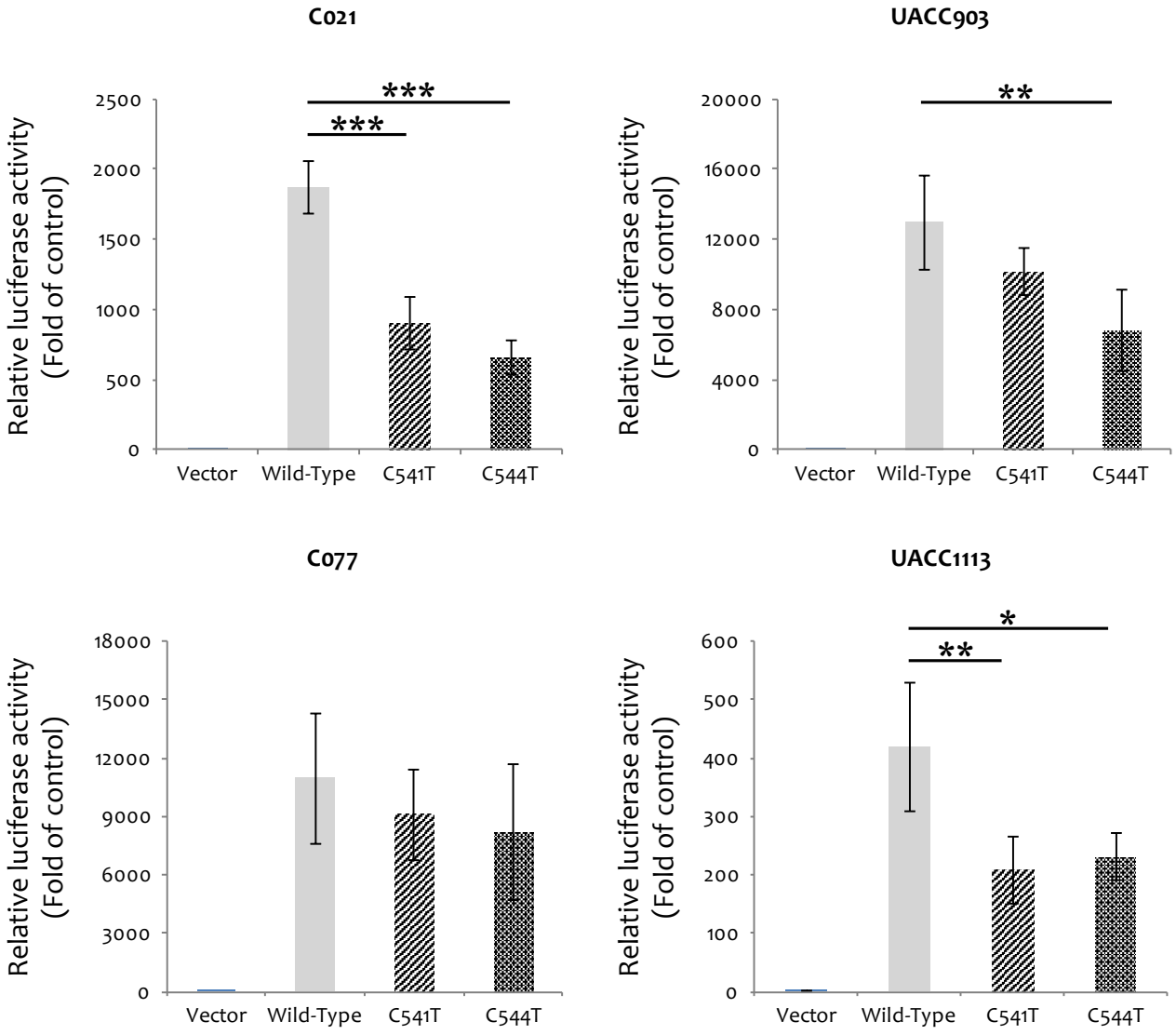
Supplementary Figure 2. *SDHD* expression difference in melanomas harboring promoter mutations compared to *SDHD* wild-type samples. *SDHD* promoter-mutant samples are grouped according to mutation. *SDHD* expression was significantly decreased in the set of tumors harboring the *SDHD* C523T promoter mutation (one-tailed student's t-test, $P = 0.0135$) compared to wild-type samples. "Other Hotspot Mutation" includes the *SDHD* promoter mutations C532A, C541T, C544T and C548T, while "Non-Hotspot Mutation" includes *SDHD* promoter mutations C515T, A530G, C531T, C547T and C549T. Copy number for each sample as predicted by GISTIC is denoted with different coloring (Purple/-2: homozygous deletion; Red/-1: shallow deletion; Green/0: copy-neutral; Blue/1: copy gain; Black/NA: not assessable).

Fig S2


SDHD Putative copy−number alterations from GISTIC
−2
−1
0
1
NA
SDHD mRNA expression (RNA Seq V2 RSEM) (log2)
12
11
10
9
8
C523T Mutation
Other Hotspot Mutations
Other Non−Hotspot Mutations
Wild−Type

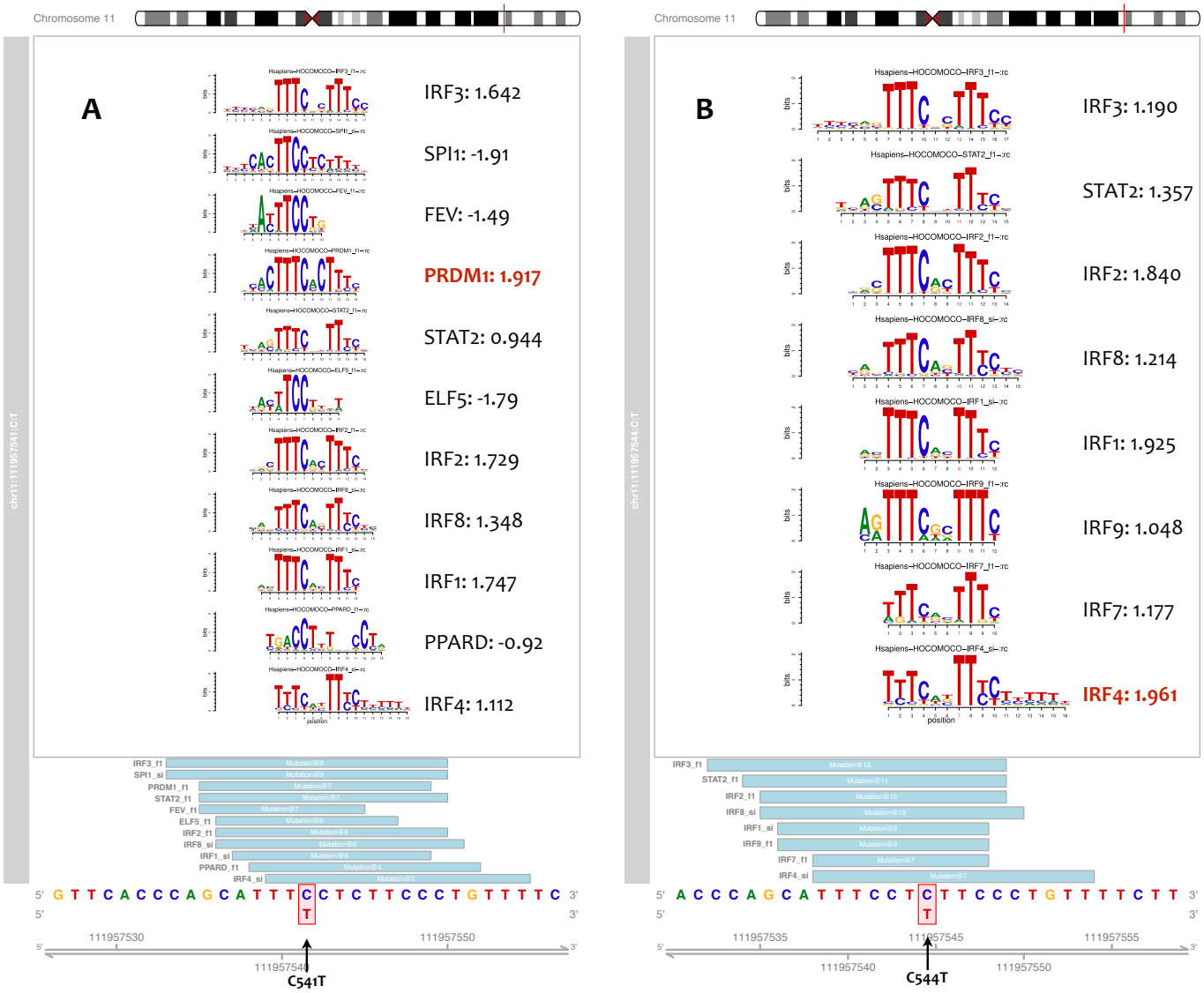
Supplementary Figure 3. *SDHD* promoter activity is significantly decreased by the C541T and C544T *SDHD* hotspot mutations in multiple melanoma cell lines. A 163 bp fragment from the wild-type *SDHD* promoter sequence surrounding hotspot mutations significantly enhance luciferase reporter expression relative to vector control, whereas the same fragment containing hotspot mutations decrease enhancer activity relative to the wild-type sequence. Luciferase activity was measured 24hr after transfection and normalized to Renilla luciferase readings. Fold change over minimal promoter control (vector only) is plotted as relative luciferase activity. The experiment was performed four times with triplicates for each. Stars denote significant differences in luciferase activity by two-tailed student's t-test (*: *P*-value <0.05; **: *P*-value <0.01; ***: *P*-value <0.001).

Fig S3


C021
Relative luciferase activity (Fold of control)
2500
2000
1500
1000
500
0
***
***
Vector
Wild-Type
C541T
C544T
UACC903
Relative luciferase activity (Fold of control)
20000
16000
12000
8000
4000
0
**
Vector
Wild-Type
C541T
C544T
C077
Relative luciferase activity (Fold of control)
18000
15000
12000
9000
6000
3000
0
Vector
Wild-Type
C541T
C544T
UACC1113
Relative luciferase activity (Fold of control)
600
500
400
300
200
100
0
*
**
Vector
Wild-Type
C541T
C544T

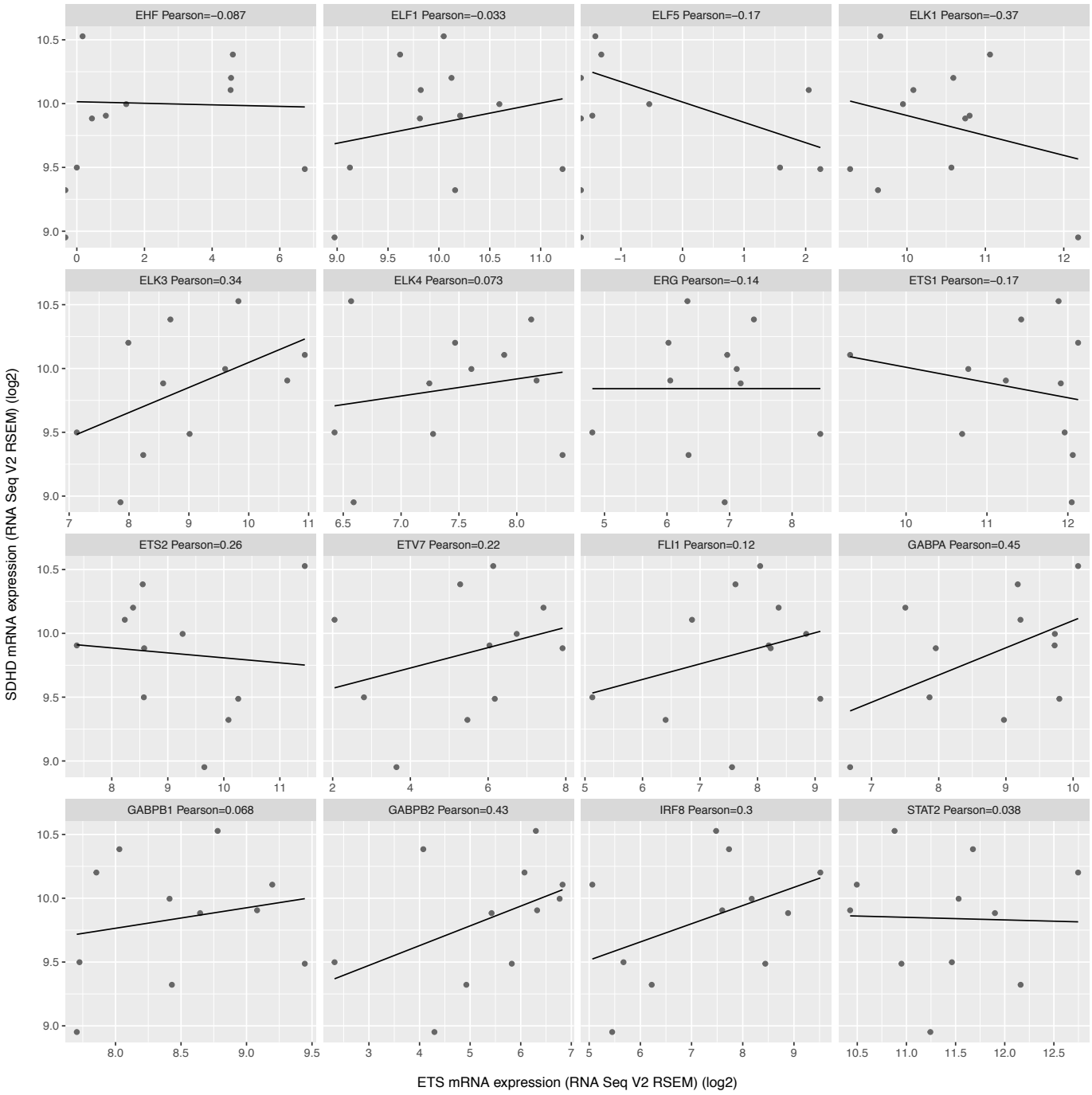
Supplementary Figure 4. Predicting *SDHD* promoter mutation effects on transcription factor binding sites. Data are shown for **(A)** C541T and **(B)** C544T. Genomic sequence and coordinates are at the bottom of the display; the positions of the matches represented (light blue boxes). The position of the mutations within the motif is indicated by a red-bounded box, with the alternate allele below in red font as on the motif logo position bar above. The motif logos generated from *motfstack* are shown above using the color conventions of the genomic sequence below. Predicted transcription factor name and change score (Alterscore-Refscore) are shown to the right of each motif, and the transcription factor with the strongest score is highlighted in red. Mutations leading to disruption of transcription factor binding sites have negative change scores, while those creating new transcription factor binding sites have positive change scores.

Fig S4


A
Chromosome 11
chr11:111957541:C:T
IRF3: 1.642
SPI1: -1.91
FEV: -1.49
PRDM1: 1.917
STAT2: 0.944
ELF5: -1.79
IRF2: 1.729
IRF8: 1.348
IRF1: 1.747
PPARD: -0.92
IRF4: 1.112
position
IRF3_f1
SPI1_si
PRDM1_f1
STAT2_f1
FEV_f1
ELF5_f1
IRF2_f1
IRF8_si
IRF1_si
PPARD_f1
IRF4_si
5' G T T C A C C C A G C A T T T C C T C T T C C C T G T T T T C 3'
5' T 3'
111957530
111957550
111957540
C541T
B
Chromosome 11
chr11:111957544:C:T
IRF3: 1.190
STAT2: 1.357
IRF2: 1.840
IRF8: 1.214
IRF1: 1.925
IRF9: 1.048
IRF7: 1.177
IRF4: 1.961
position
IRF3_f1
STAT2_f1
IRF2_f1
IRF8_si
IRF1_si
IRF9_f1
IRF7_f1
IRF4_si
5' A C C C A G C A T T T C C T C T T C C C C T G T T T T C T T 3'
5' T 3'
111957535
111957545
111957555
111957540
111957550
C544T

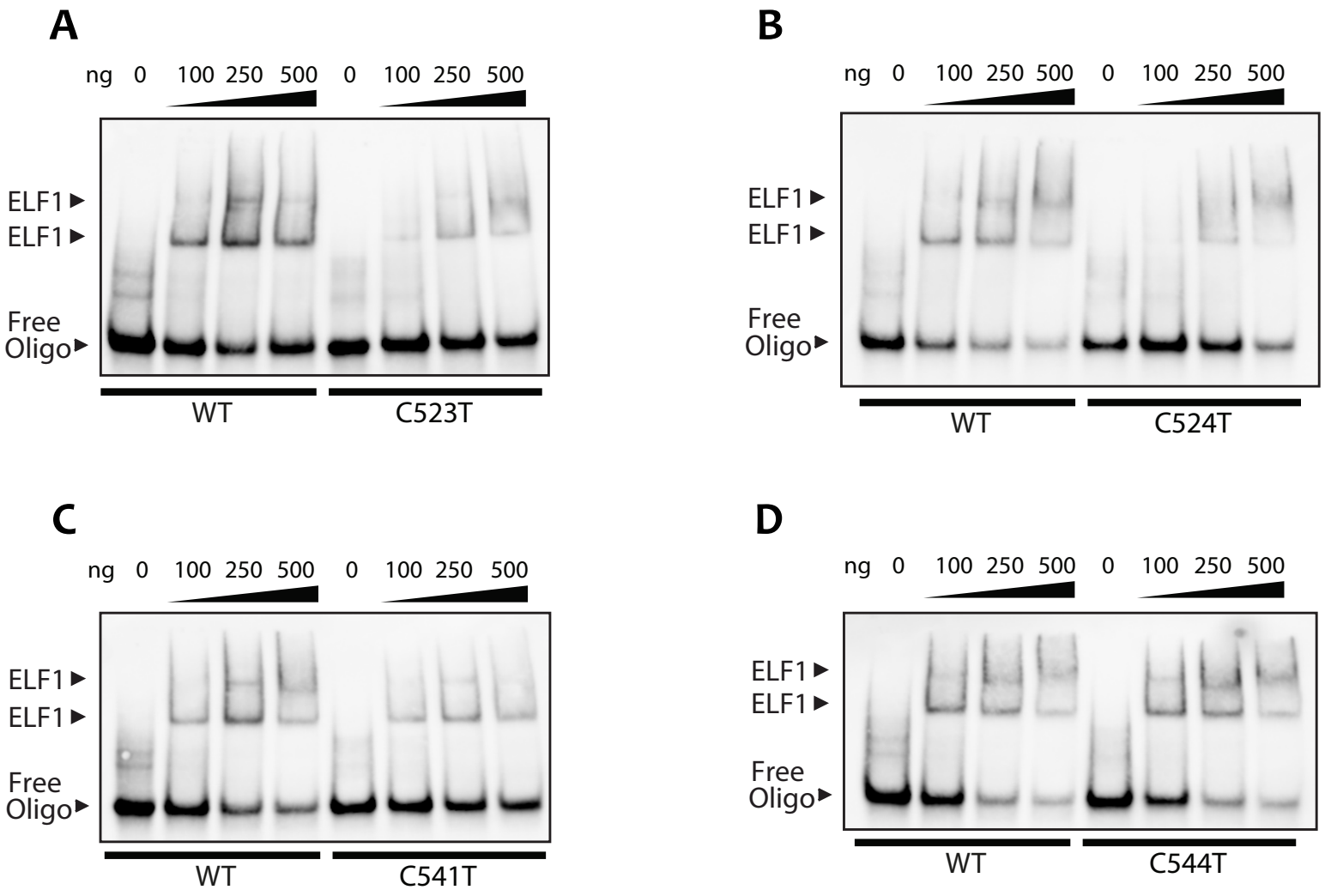
Supplementary Figure 5. mRNA expression correlation between *SDHD* and multiple ETS transcription factors in TCGA SKCM samples harboring the *SDHD* C523T promoter mutation. Pearson correlation of mRNA expression between *SDHD* and 16 transcription factors with consensus motifs altered by the C523T mutation as predicted by *motifbreakR*. Significant Pearson correlations are highlighted with one or more star (*: *P*-value <0.05; **: *P*-value <0.01; ***: *P*-value <0.001).

Fig S5


EHF Pearson=−0.087
ELF1 Pearson=−0.033
ELF5 Pearson=−0.17
ELK1 Pearson=−0.37
ELK3 Pearson=0.34
ELK4 Pearson=0.073
ERG Pearson=−0.14
ETS1 Pearson=−0.17
ETS2 Pearson=0.26
ETV7 Pearson=0.22
FLI1 Pearson=0.12
GABPA Pearson=0.45
GABPB1 Pearson=0.068
GABPB2 Pearson=0.43
IRF8 Pearson=0.3
STAT2 Pearson=0.038
SDHD mRNA expression (RNA Seq V2 RSEM) (log2)
ETS mRNA expression (RNA Seq V2 RSEM) (log2)

Supplementary Figure 6. Band-shift experiments indicate wild-type specific binding of ELF1 to the *SDHD* promoter. (A) Band-shift analysis with the C523T *SDHD* promoter mutation oligo and recombinant human ELF1 protein. **(B)** Band-shift analysis with the C524T *SDHD* promoter mutation oligo and recombinant human ELF1 protein. **(C)** Band-shift analysis with the C541T *SDHD* promoter mutation oligo and recombinant human ELF1 protein. **(D)** Band-shift analysis with the C544T *SDHD* promoter mutation oligo and recombinant human ELF1 protein.

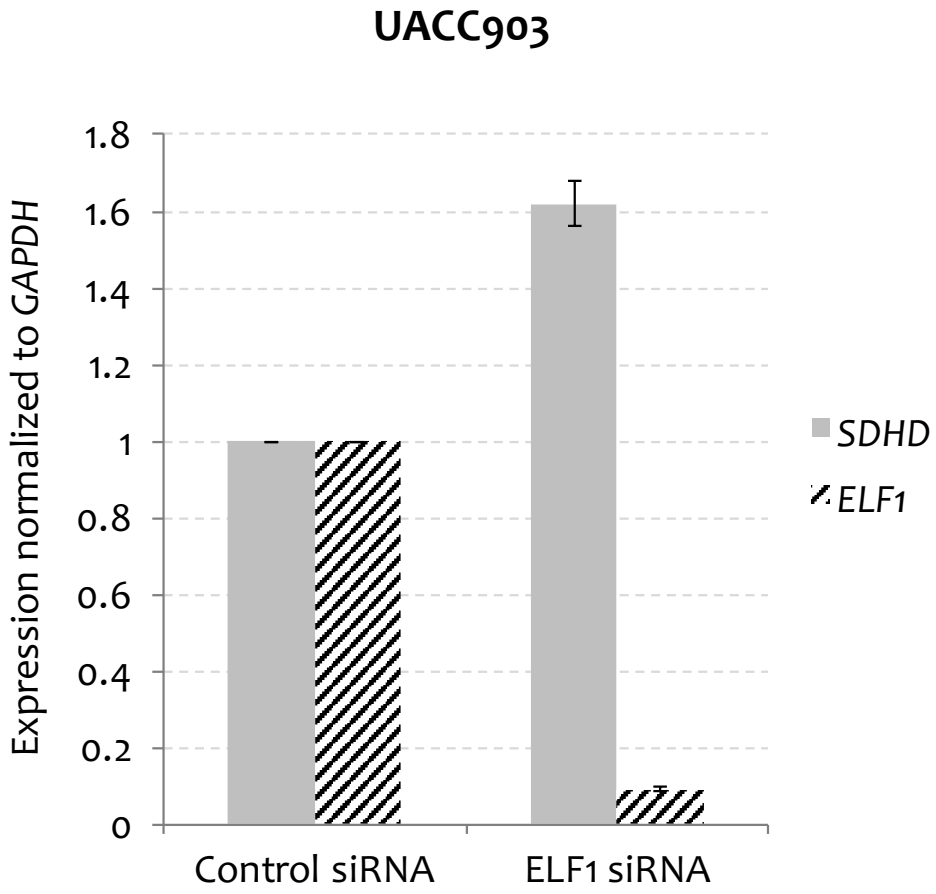
Fig S6


A
ng 0 100 250 500 0 100 250 500
ELF1
ELF1
Free Oligo
WT
C523T
B
ng 0 100 250 500 0 100 250 500
ELF1
ELF1
Free Oligo
WT
C524T
C
ng 0 100 250 500 0 100 250 500
ELF1
ELF1
Free Oligo
WT
C541T
D
ng 0 100 250 500 0 100 250 500
ELF1
ELF1
Free Oligo
WT
C544T

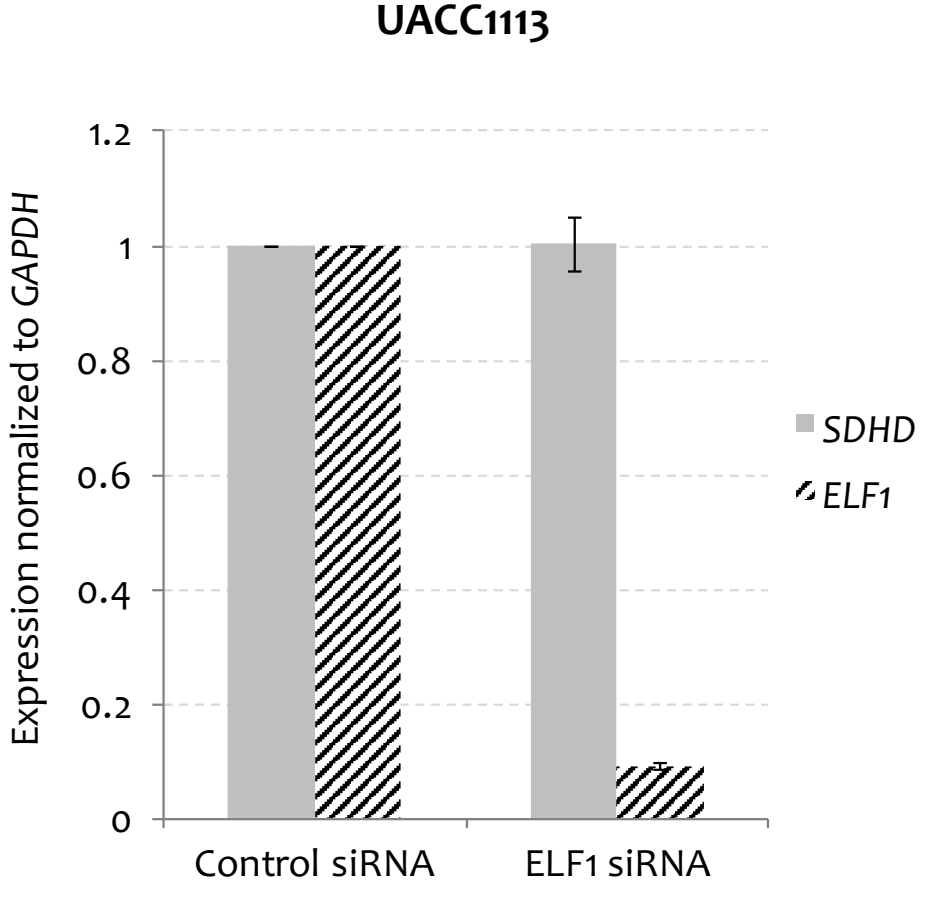
Supplementary Figure 7. siRNA-mediated knockdown of *ELF1* does not lead to decreased *SDHD* expression in melanoma cells. Control siRNA or siRNAs targeting *ELF1* were transfected into cells, and expression of *ELF1* and *SDHD* were assayed by Taqman assays at day 5 following transfection. Data are shown for two melanoma cell lines, (**A**) UACC903 and (**B**) UACC1113.

Fig S7

A

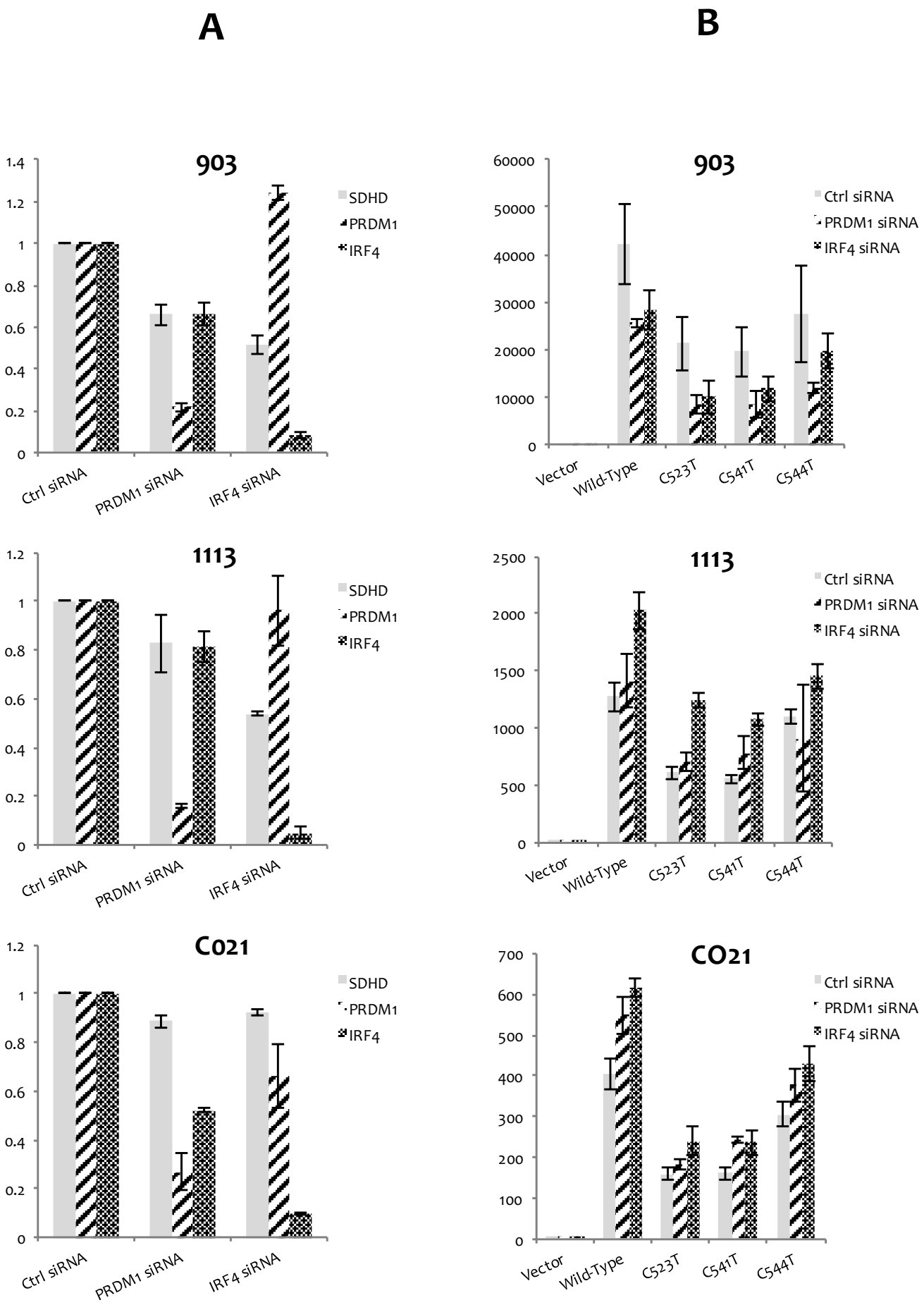

UACC903
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
Expression normalized to GAPDH
Control siRNA
ELF1 siRNA
SDHD
ELF1

B


UACC1113
1.2
1
0.8
0.6
0.4
0.2
0
Expression normalized to GAPDH
Control siRNA
ELF1 siRNA
SDHD
ELF1

Supplementary Figure 8. Effects of siRNA-mediated knockdown of *PRDM1* or *IRF4* on *SDHD* expression and *SDHD* promoter activity in melanoma cells. (**A**) Depletion of *PRDM1* or *IRF4* resulted in varied levels of reduction in *SDHD* expression across melanoma cell lines (UACC903, UACC1113, and C021). Control siRNA or siRNAs targeting *PRDM1* or *IRF4* were transfected into cells, and expression of *PRDM1*, *IRF4* and *SDHD* were assayed by Taqman assays at day five following transfection. (**B**) siRNA-mediated depletion of *PRDM1* or *IRF4* do not dramatically alter wild-type or mutant *SDHD* promoter activity in an allele-specific manner. A 163-bp fragment from the wild-type *SDHD* promoter sequence surrounding hotspot mutations significantly enhances luciferase reporter expression relative to vector control. The same fragment containing hotspot mutations results in decreased promoter activity relative to the wild-type sequence. While depletion of *PRDM1* or *IRF4* do broadly result in small alterations in reporter activity, neither alters reporter expression of these constructs in an allele-specific manner. Fold change over minimal promoter control (vector only) is plotted as relative luciferase activity. The experiment was performed four times with triplicates for each.

Fig S8


A
B
903
SDHD
PRDM1
IRF4
Ctrl siRNA
PRDM1 siRNA
IRF4 siRNA
1113
C021
903
Ctrl siRNA
PRDM1 siRNA
IRF4 siRNA
Vector
Wild-Type
C523T
C541T
C544T
1113
CO21

Supplementary Table 1. *SDHD* promoter mutations identified in melanoma tumors datasets (TCGA, Broad and Yale) and melanoma cell lines.

S1 Table. *SDHD* promoter mutations identified in melanoma tumors datasets (TCGA, Broad and Yale) and melanoma cell lines.

Chromosome	Location	Ref	Alt	Sample	Source	Ref_bases_num	Alt_bases_num
11	111957518	G	A	Ma-Mel-114	Broad	24	16
11	111957527	T	C	Ma-Mel-35	Broad	12	3
11	111957529	C	T	JWCI-WGS-21	Broad	0	7
11	111957547	C	T	ME014	Broad	20	13
11	111957515	C	T	UACC257	Cell lines	257	12
11	111957517	C	T	C021	Cell lines	59	53
11	111957524	C	T	UACC1451	Cell lines	181	5
11	111957524	C	T	UACC2528	Cell lines	138	5
11	111957524	C	T	UACC952	Cell lines	78	83
11	111957541	C	T	C021	Cell lines	54	50
11	111957541	C	T	C077	Cell lines	35	11
11	111957544	C	T	C077	Cell lines	20	12
11	111957549	C	T	C025	Cell lines	8	19
11	111957556	C	T	C088	Cell lines	61	37
11	111957515	C	T	TCGA-EE-A29M	TCGA	8	10
11	111957523	C	T	TCGA-D3-A51G	TCGA	16	5
11	111957523	C	T	TCGA-D3-A8GI	TCGA	13	3
11	111957523	C	T	TCGA-D9-A1JW	TCGA	11	7
11	111957523	C	T	TCGA-DA-A1IC	TCGA	1	6
11	111957523	C	T	TCGA-EE-A29D	TCGA	6	3
11	111957523	C	T	TCGA-EE-A2GO	TCGA	13	8
11	111957523	C	T	TCGA-EE-A3J5	TCGA	8	3
11	111957523	C	T	TCGA-HR-A2OG	TCGA	5	6
11	111957523	C	T	TCGA-IH-A3EA	TCGA	4	4
11	111957523	C	T	TCGA-W3-AA1V	TCGA	7	4
11	111957523	C	T	TCGA-YD-A9TA	TCGA	3	6
11	111957530	A	G	TCGA-EB-A5UL	TCGA	18	3
11	111957531	C	T	TCGA-EE-A2GU	TCGA	8	5
11	111957532	C	A	TCGA-D3-A2JC	TCGA	12	3
11	111957532	C	A	TCGA-EE-A2A2	TCGA	165	3
11	111957532	C	A	TCGA-ER-A19B	TCGA	8	3
11	111957541	C	T	TCGA-EE-A2MD	TCGA	7	6
11	111957541	C	T	TCGA-EE-A2MI	TCGA	11	6
11	111957541	C	T	TCGA-FS-A1ZK	TCGA	0	8
11	111957544	C	T	TCGA-EE-A185	TCGA	6	7
11	111957544	C	T	TCGA-GN-A26C	TCGA	7	10
11	111957544	C	T	TCGA-W3-AA1Q	TCGA	12	8
11	111957547	C	T	TCGA-GN-A266	TCGA	12	9
11	111957548	C	T	TCGA-D3-A2JE	TCGA	21	8
11	111957548	C	T	TCGA-FR-A8YC	TCGA	2	9
11	111957549	C	T	TCGA-GN-A26C	TCGA	8	10
11	111957517	C	T	YUPADI	Yale	13	18
11	111957523	C	T	YUGEN8	Yale	0	43
11	111957523	C	T	YURIF	Yale	15	18
11	111957524	C	T	YUROO	Yale	16	23
11	111957535	G	T	YUFOLD	Yale	92	4
11	111957544	C	T	YUKLAB	Yale	60	29
11	111957544	C	T	YURUS	Yale	40	6
11	111957548	C	T	YUZEAL	Yale	14	28

Supplementary Table 2. MotifBreakR results predicting the effects of recurrent *SDHD* promoter mutations (C523T, C524T, C541T, C544T, and C548T) on transcription factor binding sites.

S2 Table. MotifBreakR results predicting the effects of recurrent *SDHD* promoter mutations (C523T, C524T, C541T, C544T and C548T) on transcription factor binding sites.

REF	ALT	snpPos	motifPos	geneSymbol	dataSource	providerName	providerId	seqMatch	pctRef	pctAlt	scoreRef	scoreAlt	Refpvalue	Altpvalue	alleleRef	alleleAlt	effect	dscore	dpct
C	T	111957544	10	IRF4	HOCOMOCO	IRF4_si	IRF4_HUMAN	tttcctCttccctgtt	0.749	0.931	8.314	10.276	2.406E-03	4.231E-06	0.001	0.998	strong	1.961	0.182
C	T	111957544	4	IRF1	HOCOMOCO	IRF1_si	IRF1_HUMAN	catttcctCttc	0.809	0.961	10.412	12.337	8.883E-04	2.271E-05	0.000	1.000	strong	1.925	0.152
C	T	111957541	8	PRDM1	HOCOMOCO	PRDM1_f1	PRDM1_HUMAN	gcatttCctcttcc	0.734	0.859	11.437	13.354	1.073E-03	4.125E-05	0.001	0.994	strong	1.917	0.125
C	T	111957544	5	IRF2	HOCOMOCO	IRF2_f1	IRF2_HUMAN	gcatttcctCttcc	0.790	0.934	10.294	12.135	8.060E-04	1.904E-05	0.000	0.995	strong	1.841	0.144
C	T	111957541	8	IRF1	HOCOMOCO	IRF1_si	IRF1_HUMAN	atttCctcttcc	0.782	0.919	10.065	11.812	1.455E-03	6.670E-05	0.017	0.983	strong	1.747	0.138
C	T	111957541	9	IRF2	HOCOMOCO	IRF2_f1	IRF2_HUMAN	catttCctcttccc	0.742	0.878	9.683	11.412	1.741E-03	7.600E-05	0.016	0.984	strong	1.730	0.135
C	T	111957541	9	IRF3	HOCOMOCO	IRF3_f1	IRF3_HUMAN	cagcatttCctcttccc	0.737	0.879	8.831	10.474	1.852E-03	6.460E-05	0.018	0.982	strong	1.642	0.142
C	T	111957544	5	STAT2	HOCOMOCO	STAT2_f1	STAT2_HUMAN	agcatttcctCttcc	0.760	0.907	7.258	8.616	1.963E-03	4.840E-05	0.031	0.928	strong	1.358	0.147
C	T	111957523	10	IRF8	HOCOMOCO	IRF8_si	IRF8_HUMAN	gacttCcggttcacc	0.748	0.885	7.629	8.977	2.225E-03	8.056E-05	0.055	0.945	strong	1.348	0.137
C	T	111957541	10	IRF8	HOCOMOCO	IRF8_si	IRF8_HUMAN	catttCctcttccct	0.805	0.943	8.194	9.542	6.155E-04	1.085E-05	0.055	0.945	strong	1.348	0.137
C	T	111957544	6	IRF8	HOCOMOCO	IRF8_si	IRF8_HUMAN	gcatttcctCttccc	0.809	0.933	8.232	9.447	5.572E-04	1.760E-05	0.030	0.922	strong	1.214	0.124
C	T	111957544	5	IRF3	HOCOMOCO	IRF3_f1	IRF3_HUMAN	ccagcatttcctCttcc	0.840	0.943	10.028	11.218	1.671E-04	7.514E-06	0.041	0.913	strong	1.190	0.103
C	T	111957544	4	IRF7	HOCOMOCO	IRF7_f1	IRF7_HUMAN	tttcctCttc	0.831	0.979	6.730	7.908	1.288E-03	1.240E-05	0.000	0.897	strong	1.178	0.149
C	T	111957541	14	IRF4	HOCOMOCO	IRF4_si	IRF4_HUMAN	ttCctcttcctgtttt	0.831	0.934	9.198	10.310	2.983E-04	3.393E-06	0.069	0.890	strong	1.113	0.103
C	T	111957544	4	IRF9	HOCOMOCO	IRF9_f1	IRF9_HUMAN	catttcctCttc	0.771	0.893	7.091	8.140	6.152E-04	2.259E-05	0.000	1.000	strong	1.049	0.122
C	T	111957541	9	STAT2	HOCOMOCO	STAT2_f1	STAT2_HUMAN	gcatttCctcttccc	0.818	0.920	7.793	8.737	4.709E-04	2.864E-05	0.116	0.856	strong	0.944	0.102
C	T	111957523	9	STAT2	HOCOMOCO	STAT2_f1	STAT2_HUMAN	cgacttCcggttcac	0.788	0.890	7.512	8.456	1.041E-03	8.519E-05	0.116	0.856	strong	0.944	0.102
C	T	111957548	5	FOXM1	HOCOMOCO	FOXM1_f1	FOXM1_HUMAN	cttcCctgttttc	0.852	0.920	4.940	5.312	4.527E-04	3.801E-05	0.000	0.514	weak	0.372	0.068
C	T	111957544	8	ETS2	HOCOMOCO	ETS2_f1	ETS2_HUMAN	cctCttcctg	0.980	0.928	6.361	6.037	2.861E-05	8.788E-04	0.676	0.252	weak	-0.324	-0.052
C	T	111957548	4	PPARD	HOCOMOCO	PPARD_f1	PPARD_HUMAN	tttcctcttcCctg	0.879	0.813	7.460	6.930	3.036E-05	2.651E-04	0.770	0.056	strong	-0.530	-0.065
C	T	111957544	6	SPI1	HOCOMOCO	SPI1_si	SPI1_HUMAN	cagcatttcctCttccc	0.889	0.836	11.611	10.937	5.897E-06	5.725E-05	0.787	0.108	weak	-0.673	-0.053
C	T	111957541	11	PPARD	HOCOMOCO	PPARD_f1	PPARD_HUMAN	tttCctcttccctg	0.879	0.765	7.460	6.540	3.036E-05	9.085E-04	0.882	0.062	strong	-0.920	-0.113
C	T	111957523	6	ELK3	HOCOMOCO	ELK3_f1	ELK3_HUMAN	cgacttCcggtt	0.928	0.754	6.882	5.655	5.287E-05	3.725E-03	1.000	0.000	strong	-1.227	-0.174
C	T	111957524	5	ELK3	HOCOMOCO	ELK3_f1	ELK3_HUMAN	cgacttcCggtt	0.928	0.754	6.882	5.655	5.287E-05	3.725E-03	1.000	0.000	strong	-1.227	-0.174
C	T	111957523	8	FLI1	HOCOMOCO	FLI1_f1	FLI1_HUMAN	tctcgacttCcggttca	0.968	0.785	6.753	5.520	1.795E-05	4.244E-03	0.924	0.000	strong	-1.233	-0.184
C	T	111957523	8	ETV7	HOCOMOCO	ETV7_si	ETV7_HUMAN	tctcgacttCcggttca	0.849	0.722	9.100	7.808	8.974E-05	1.963E-03	1.000	0.000	strong	-1.293	-0.127
C	T	111957524	7	ETV7	HOCOMOCO	ETV7_si	ETV7_HUMAN	tctcgacttcCggttca	0.849	0.722	9.100	7.808	8.974E-05	1.963E-03	1.000	0.000	strong	-1.293	-0.127
C	T	111957523	5	ETS2	HOCOMOCO	ETS2_f1	ETS2_HUMAN	cgacttCcggt	0.970	0.764	6.301	5.007	8.345E-05	1.436E-02	0.933	0.067	strong	-1.294	-0.206
C	T	111957548	4	ETS2	HOCOMOCO	ETS2_f1	ETS2_HUMAN	cctcttcCctg	0.980	0.768	6.361	5.034	2.861E-05	1.374E-02	0.936	0.015	strong	-1.327	-0.212
C	T	111957524	4	ETS2	HOCOMOCO	ETS2_f1	ETS2_HUMAN	cgacttcCggt	0.970	0.759	6.301	4.974	8.345E-05	1.510E-02	0.936	0.015	strong	-1.327	-0.212
C	T	111957524	4	ELK1	HOCOMOCO	ELK1_f1	ELK1_HUMAN	acttcCggt	1.000	0.816	7.395	6.055	0.000E+00	3.193E-03	0.919	0.020	strong	-1.340	-0.184
C	T	111957523	6	ELK4	HOCOMOCO	ELK4_f1	ELK4_HUMAN	gacttCcggtt	0.999	0.868	10.671	9.283	1.192E-06	2.401E-04	0.945	0.045	strong	-1.388	-0.131
C	T	111957524	7	FLI1	HOCOMOCO	FLI1_f1	FLI1_HUMAN	tctcgacttcCggttca	0.968	0.760	6.753	5.353	1.795E-05	6.113E-03	0.962	0.038	strong	-1.400	-0.209
C	T	111957541	4	FEV	HOCOMOCO	FEV_f1	FEV_HUMAN	gcatttCctc	0.957	0.779	8.291	6.792	7.153E-05	3.216E-03	1.000	0.000	strong	-1.498	-0.178
C	T	111957523	15	TFCP2	HOCOMOCO	TFCP2_f1	TFCP2_HUMAN	tCcggttcacccagca	0.903	0.662	5.881	4.383	6.354E-05	2.268E-02	1.000	0.000	strong	-1.498	-0.242
C	T	111957524	5	ELK4	HOCOMOCO	ELK4_f1	ELK4_HUMAN	gacttcCggtt	0.999	0.853	10.671	9.128	1.192E-06	3.133E-04	0.963	0.010	strong	-1.544	-0.146
C	T	111957524	3	GABPB1+GABPB2	HOCOMOCO	GABP1+GABP2_f1	GABP1+GABP2_HUMAN	cgacttcCgg	0.987	0.807	8.641	7.096	1.049E-05	2.362E-03	0.973	0.027	strong	-1.544	-0.180
C	T	111957523	8	EHF	HOCOMOCO	EHF_si	EHF_HUMAN	gacttCcggttca	0.939	0.811	11.452	9.905	8.956E-06	7.288E-04	0.940	0.000	strong	-1.547	-0.128
C	T	111957523	5	ELK1	HOCOMOCO	ELK1_f1	ELK1_HUMAN	acttCcggt	1.000	0.783	7.395	5.811	0.000E+00	5.070E-03	0.959	0.013	strong	-1.584	-0.217
C	T	111957523	4	GABPB1+GABPB2	HOCOMOCO	GABP1+GABP2_f1	GABP1+GABP2_HUMAN	cgacttCcgg	0.987	0.780	8.641	6.865	1.049E-05	4.217E-03	1.000	0.000	strong	-1.776	-0.207
C	T	111957523	6	ELF5	HOCOMOCO	ELF5_f1	ELF5_HUMAN	gacttCcggtt	0.952	0.723	7.604	5.814	6.890E-05	1.560E-02	1.000	0.000	strong	-1.790	-0.229
C	T	111957524	5	ELF5	HOCOMOCO	ELF5_f1	ELF5_HUMAN	gacttcCggtt	0.952	0.723	7.604	5.814	6.890E-05	1.560E-02	1.000	0.000	strong	-1.790	-0.229
C	T	111957541	6	ELF5	HOCOMOCO	ELF5_f1	ELF5_HUMAN	catttCctctt	0.970	0.742	7.745	5.955	2.480E-05	1.425E-02	1.000	0.000	strong	-1.790	-0.229
C	T	111957523	5	ELF1	HOCOMOCO	ELF1_f1	ELF1_HUMAN	gacttCcggt	0.997	0.788	9.083	7.203	6.676E-06	4.254E-03	1.000	0.000	strong	-1.881	-0.209
C	T	111957524	4	ELF1	HOCOMOCO	ELF1_f1	ELF1_HUMAN	gacttcCggt	0.997	0.788	9.083	7.203	6.676E-06	4.254E-03	1.000	0.000	strong	-1.881	-0.209
C	T	111957523	5	ETS1	HOCOMOCO	ETS1_si	ETS1_HUMAN	acttCcggt	0.985	0.743	7.821	5.925	1.526E-05	1.568E-02	0.996	0.000	strong	-1.896	-0.243
C	T	111957541	9	SPI1	HOCOMOCO	SPI1_si	SPI1_HUMAN	cagcatttCctcttccc	0.889	0.739	11.611	9.698	5.897E-06	1.082E-03	0.994	0.005	strong	-1.913	-0.150
C	T	111957524	4	ETS1	HOCOMOCO	ETS1_si	ETS1_HUMAN	acttcCggt	0.985	0.738	7.821	5.887	1.526E-05	1.577E-02	1.000	0.000	strong	-1.934	-0.247
C	T	111957524	7	EHF	HOCOMOCO	EHF_si	EHF_HUMAN	gacttcCggttca	0.939	0.776	11.452	9.487	8.956E-06	1.537E-03	1.000	0.000	strong	-1.966	-0.163
C	T	111957523	5	ERG	HOCOMOCO	ERG_f1	ERG_HUMAN	cgacttCcggt	0.983	0.811	11.372	9.392	1.907E-06	9.186E-04	1.000	0.000	strong	-1.980	-0.172
C	T	111957524	4	ERG	HOCOMOCO	ERG_f1	ERG_HUMAN	cgacttcCggt	0.983	0.811	11.372	9.392	1.907E-06	9.186E-04	1.000	0.000	strong	-1.980	-0.172
C	T	111957523	7	GABPA	HOCOMOCO	GABPA_f1	GABPA_HUMAN	cgacttCcggttc	0.983	0.820	12.201	10.205	3.353E-06	7.427E-04	1.000	0.000	strong	-1.995	-0.162
C	T	111957524	6	GABPA	HOCOMOCO	GABPA_f1	GABPA_HUMAN	cgacttcCggttc	0.983	0.820	12.201	10.205	3.353E-06	7.427E-04	1.000	0.000	strong	-1.995	-0.162

Note:
REF :the reference allele for the SNP
ALT :the alternate allele for the SNP
snpPos :the coordinates of the SNP
motifPos :the coordinates of the SNP within the TF binding motif
geneSymbol :the geneSymbol corresponding to the TF of the TF binding motif
dataSource :the source of the TF binding motif
providerName, providerId :the name and id provided by the source
seqMatch :the sequence on the 5' -> 3' direction of the "+" strand that corresponds to DNA at the position that the TF binding motif was found.
pctRef :The score as determined by the scoring method, when the sequence contains the reference SNP allele, normalized to a scale from 0 - 1. If filterp = FALSE, this is the value that is thresholded.
pctAlt :The score as determined by the scoring method, when the sequence contains the alternate SNP allele, normalized to a scale from 0 - 1. If filterp = FALSE, this is the value that is thresholded.
scoreRef :The score as determined by the scoring method, when the sequence contains the reference SNP allele
scoreAlt :The score as determined by the scoring method, when the sequence contains the alternate SNP allele
Refpvalue :p-value for the match for the pctRef score, initially set to NA. see calculatePvalue for more information
Altpvalue :p-value for the match for the pctAlt score, initially set to NA. see calculatePvalue for more information
alleleRef :The proportional frequency of the reference allele at position motifPos in the motif
alleleAlt :The proportional frequency of the alternate allele at position motifPos in the motif
effect :one of weak, strong, or neutral indicating the strength of the effect.
dscore: scoreAlt-ScoreRef
dpct: pctAlt-pctRef

Supplementary Table 3. Oligonucleotide design for quantitative mass spectrometry.

S3 Table. Oligonucleotide design for quantitative mass spectrometry.

Oligo name	Forward	Reverse
WT_SDHD	5′-GTGCACCGCCTCTCGACTTCcGGTTCACCCAGCATTTcCTcTTCCCTGTTTTCTTTCGTCG-3′	5′- CGACGAAAGAAAACAGGGAAgAGgAAATGCTGGGTGAACCgGAAGTCGAGAGGCGGTGCAC-3′
C524T	5′-GTGCACCGCCTCTCGACTTCtGGTTCACCCAGCATTTCCTCTTCCCTGTTTTCTTTCGTCG-3′	5′-CGACGAAAGAAAACAGGGAAGAGGAAATGCTGGGTGAACCaGAAGTCGAGAGGCGGTGCAC-3′
C541T	5′-GTGCACCGCCTCTCGACTTCCGGTTCACCCAGCATTTtCTCTTCCCTGTTTTCTTTCGTCG-3′	5′-CGACGAAAGAAAACAGGGAAGAGaAAATGCTGGGTGAACCGGAAGTCGAGAGGCGGTGCAC-3′
C544T	5′-GTGCACCGCCTCTCGACTTCCGGTTCACCCAGCATTTCCTtTTCCCTGTTTTCTTTCGTCG-3′	5′- CGACGAAAGAAAACAGGGAAaAGGAAATGCTGGGTGAACCGGAAGTCGAGAGGCGGTGCAC-3′

Design Location: chr11:111,957,504-111,957,564