Figure 1. Chromosomal location of the 273 genes related to epigenetic regulation. The DD genes were indicated with green arrow, UU genes with violet arrow on left -hand side, whereas the non-DD UU genes with red arrows on right-hand side. The chromosome regions significantly enriched in genes related to epigenetic regulation, which were identified using positional gene enrichment analysis [9], were indicated with orange boxes.

Fig.2 Regulatory sequence analysis of epigenetic genes. Seven well-characterized BRAFV600E signaling transcription factors (TFs), including CREB1, Elk-1, c-Fos, myc, STAT1, STAT2 and PPARγ, were analyzed. Sequences ranging over 3 kbp upstream and 1.5 kbp downstream of the transcription start site of each epigenetic gene were retrieved from EnsEMBL human genome (GRCh37) (www.ensembl.org). The regulatory sequence analysis tools (RSAT) [30] was used for scan for the binding motifs of the 7 TFs. The position weight matrix for the transcription factors were extracted from Jaspar vertebrate redundant database (http://jaspar.cgb.ki.se). To minimize the false positive rate, threshold on 'p-value' was set to 5×10^{-5} for RSAT analysis. **A)** Average number of TF binding motifs in the 3 groups of epigenetic genes**. B)** The percentage of genes that harbor the TF binding motif in their promoter regions in the 3 groups of epigenetic genes**.**

Fig. 3 Randomization test for Pearson's r values. A) Random distribution of the Pearson's r of the expression level of the epigenetic genes to the expression of the 11 potential TSGs in melanoma cells. Since there are totally 20,119 r values (77 per one epigenetic gene) for Pearson correlation analysis of the expression of the 273 epigenetic genes to the expression of the 11 TSGs in the 7 microarray datasets, 77 numerical numbers were randomly picked from 20,119 Pearson's r values, and the median values of the 77 numerical numbers were counted. The procedures were repeated 200,000 times, and a frequency histogram was created by tracking the median values. Red lines represent the 5th and 95th percentiles. The arrows show the median value of the 77 Pearson's r for individual DD and UU genes. The number of times (T) of which the random median values were higher than the actual median number of a DD gene or less than the actual median number of a UU gene were counted, and the p value for an

individual DD or UU gene was calculated using the formula *(1-T/200000)*. **B)** Random distribution of the Pearson's r of the expression of the epigenetic genes to the methylation level of the 31 potential TSGs. Similar procedure was used as described in **(A)**, except that in this case we randomly picked 31 numerical numbers from 8,184 r values generated by the Pearson correlation analysis of the expression of the epigenetic genes to the methylation level of the 31 TSGs in melanoma cells.

Fig. 4 Comparison of Pearson's r values of DD gene expression to TSG expression and r values of DD gene expression to TSG methylation. Eleven DD genes that showed significantly negative correlation with the TSG expression were included in this analysis. Shown on the left axes are the Pearson's r values of the expression of the DD genes to the methylation level of the TSGs, and shown on the right axes are the r values of the expression of the DD genes to the expression level of the TSGs.

Table 1. List of 273 epigenetic genes

Gene Symbol	Gene Name	Reference
	DNA methylaiton	
AICDA	activation-induced cytidine deaminase	GO:0080111
ALKBH1	alkB, alkylation repair homolog 1	GO:0080111
ALKBH2	alkB, alkylation repair homolog 2	GO:0080111
APEX1	APEX nuclease (multifunctional DNA repair enzyme) 1	GO:0080111
APOBEC1	apolipoprotein B mRNA editing enzyme, catalytic polypeptide 1	GO:0080111
APOBEC2	apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 2	GO:0080111
APOBEC3A	apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3A	GO:0080111
APOBEC3C	apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3C	GO:0080111
APOBEC3F	apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3F	GO:0080111
ATF7IP	activating transcription factor 7 interacting protein	GO:0006306
ATRX	alpha thalassemia/mental retardation syndrome X-linked	GO:0006306
BAZ2A	bromodomain adjacent to zinc finger domain, 2A	GO:0006306
DMAP1	DNA methyltransferase 1 associated protein 1	GO:0006306
DNMT1	DNA (cytosine-5-)-methyltransferase 1	GO:0009008, GO:0003886, GO:0006306
DNMT3A	DNA (cytosine-5-)-methyltransferase 3 alpha	GO:0003886, GO:0051718, GO:0006306
DNMT3B	DNA (cytosine-5-)-methyltransferase 3 beta	GO:0003886, GO:0051718, GO:0009008, GO:0006306
DNMT3L	DNA (cytosine-5-)-methyltransferase 3-like	GO:0006306
FTO	fat mass and obesity associated	GO:0080111
GNAS	GNAS complex locus	GO:0006306
HEMK1	HemK methyltransferase family member 1	GO:0006306
MGMT	O-6-methylguanine-DNA methyltransferase	GO:0009008, GO:0006306
TET1	tet methylcytosine dioxygenase 1	GO:0080111
TRDMT1	tRNA aspartic acid methyltransferase 1	GO:0003886, GO:0006306
	Methyl-CpG binding	
LRWD1	leucine-rich repeats and WD repeat domain containing 1	GO:0008327
MBD1	methyl-CpG binding domain protein 1	GO:0008327
MBD2	methyl-CpG binding domain protein 2	GO:0008327, GO:0000118
MBD3	methyl-CpG binding domain protein 3	GO:0016581
MBD4	methyl-CpG binding domain protein 4	[18]
MECP2	methyl CpG binding protein 2	[18]
UHRF1	ubiquitin-like with PHD and ring finger domains 1	GO:0008327
ZBTB33	zinc finger and BTB domain containing 33	[20]
ZNF295	zinc finger protein 295	GO:0008327
	Histone acetyltion	
ATF2	activating transcription factor 2	[18]
BRCA2	breast cancer 2, early onset	GO:0010484, GO:0010485
CDY1	chromodomain protein, Y-linked, 1	GO:0004402
CDY2B	chromodomain protein, Y-linked, 2B	GO:0004402
CDYL	chromodomain protein, Y-like	GO:0004402
CLOCK	clock homolog	GO:0004402
CREBBP	CREB binding protein	GO:0004402, GO:0000123
CSRP2BP	CSRP2 binding protein	GO:0004402
ELP3	elongation protein 3 homolog	GO:0004402

ELP4	elongation protein 4 homolog	GO:0004402
EP300	E1A binding protein p300	GO:0004402, GO:0000123
EPC1	enhancer of polycomb homolog 1	GO:0004402
GTF3C4	general transcription factor IIIC, polypeptide 4	GO:0004402
HAT1	histone acetyltransferase 1	GO:0004402
HCFC1	host cell factor C1 (VP16-accessory protein)	GO:0000123
ING3	inhibitor of growth family, member 3	GO:0004402
ING4	inhibitor of growth family, member 4	GO:0000123
KANSL1	KAT8 regulatory NSL complex subunit 1	GO:0000123
KANSL2	KAT8 regulatory NSL complex subunit 2	GO:0000123
KANSL3	KAT8 regulatory NSL complex subunit 3	GO:0000123
KAT2A	K(lysine) acetyltransferase 2A	GO:0004402, GO:0010484, GO:0043997
KAT2B	K(lysine) acetyltransferase 2B	GO:0004402, GO:0016585
KAT5	K(lysine) acetyltransferase 5	GO:0004402
KAT6A	K(lysine) acetyltransferase 6A	GO:0004402
KAT6B	K(lysine) acetyltransferase 6B	GO:0004402
KAT7	K(lysine) acetyltransferase 7	GO:0004402, GO:0000123
KAT8	K(lysine) acetyltransferase 8	GO:0004402, GO:0000123
MED24	mediator complex subunit 24	GO:0004402
METTL8	methyltransferase like 8	GO:0004402
MGEA5	meningioma expressed antigen 5	GO:0004402
NAA60	N(alpha)-acetyltransferase 60, NatF catalytic subunit	GO:0010485
NCOA1	nuclear receptor coactivator 1	GO:0004402
NCOA2	nuclear receptor coactivator 2	GO:0004402
NCOA3	nuclear receptor coactivator 3	GO:0004402
OGT	O-linked N-acetylglucosamine (GlcNAc) transferase	GO:0000123
PHF15	PHD finger protein 15	GO:0000123
PHF16	PHD finger protein 16	GO:0000123
PHF17	PHD finger protein 17	GO:0000123
PHF20	PHD finger protein 20	GO:0000123
SAP130	Sin3A-associated protein, 130kDa	GO:0004402
SRCAP	Snf2-related CREBBP activator protein	GO:0004402
SUPT3H	suppressor of Ty 3 homolog	GO:0004402
SUPT7L	suppressor of Ty 7-like	GO:0004402
TADA1	transcriptional adaptor 1	GO:0004402
TADA2A	transcriptional adaptor 2A	GO:0004402
TADA3	transcriptional adaptor 3	GO:0004402
TAF1	TAF1 RNA polymerase II, TATA box binding protein (TBP)-associated factor	GO:0004402
TAF10	TAF10 RNA polymerase II, TATA box binding protein (TBP)-associated factor	GO:0004402
TAF12	TAF12 RNA polymerase II, TATA box binding protein (TBP)-associated factor	GO:0004402
TAF1L	TAF1 RNA polymerase II, TATA box binding protein (TBP)-associated factor, -like	GO:0004402
TAF5	TAF5 RNA polymerase II, TATA box binding protein (TBP)-associated factor	GO:0004402
TAF5L	TAF5-like RNA polymerase II, p300/CBP-associated factor (PCAF)-associated factor	GO:0004402
TAF6L	TAF6-like RNA polymerase II, p300/CBP-associated factor (PCAF)-associated factor	GO:0004402
TAF9	TAF9 RNA polymerase II, TATA box binding protein (TBP)-associated factor	GO:0004402
USP22	ubiquitin specific peptidase 22	GO:0010485
Histone deacetylation		

APPL1	adaptor protein, phosphotyrosine interaction, PH domain and leucine zipper containing 1	GO:0016581
APPL2	adaptor protein, phosphotyrosine interaction, PH domain and leucine zipper containing 2	GO:0016581
CBX5	chromobox homolog 5	GO:0000118
CHD3	chromodomain helicase DNA binding protein 3	GO:0016581
CHD4	chromodomain helicase DNA binding protein 4	GO:0016581
CIR1	corepressor interacting with RBPJ, 1	GO:0000118
CSNK2A1	casein kinase 2, alpha 1 polypeptide	GO:0016581,
GATAD2A	GATA zinc finger domain containing 2A	GO:0016581, GO:0006306
HDAC1	histone deacetylase 1	GO:0004407, GO:0046969, GO:0032041, GO:0046970, GO:0016581,
HDAC2	histone deacetylase 2	GO:0004407, GO:0046969, GO:0032041, GO:0046970, GO:0016581, GO:0035098
HDAC3	histone deacetylase 3	GO:0004407, GO:0046969, GO:0032041, GO:0046970
HDAC4	histone deacetylase 4	GO:0004407, GO:0046969, GO:0032041, GO:0046970
HDAC5	histone deacetylase 5	GO:0004407, GO:0046969, GO:0032041, GO:0046970
HDAC6	histone deacetylase 6	GO:0004407, GO:0046969, GO:0032041, GO:0046970
HDAC7	histone deacetylase 7	GO:0046969, GO:0032041, GO:0046970
HDAC8	histone deacetylase 8	GO:0004407, GO:0046969, GO:0032041, GO:0046970
HDAC9	histone deacetylase 9	GO:0004407, GO:0046969, GO:0032041, GO:0046970
HDAC10	histone deacetylase 10	GO:0004407, GO:0046969, GO:0032041, GO:0046970
HDAC11	histone deacetylase 11	GO:0004407, GO:0046969, GO:0032041, GO:0046970
HR	hairless homolog	GO:0000118
MECOM	MDS1 and EVI1 complex locus	GO:0000118
MTA1	metastasis associated 1	GO:0016581
MTA2	metastasis associated 1 family, member 2	GO:0004407, GO:0016581, GO:0000118
NCOR1	nuclear receptor corepressor 1	GO:0000118,
NCOR2	nuclear receptor corepressor 2	GO:0000118
NRIP1	nuclear receptor interacting protein 1	GO:0000118
PHF21A	PHD finger protein 21A	GO:0000118
RBBP4	retinoblastoma binding protein 4	GO:0016581, GO:0035098, GO:0016589, GO:0033186
RBBP7	retinoblastoma binding protein 7	GO:0016581, GO:0035098
RERE	arginine-glutamic acid dipeptide (RE) repeats	GO:0000118
SALL1	sal-like 1	GO:0004407, GO:0016581
SALL2	sal-like 2	GO:0016581
SAP18	Sin3A-associated protein	GO:0000118
SAP30	Sin3A-associated protein	GO:0000118
SATB2	SATB homeobox 2	GO:0000118
SIRT1	sirtuin 1	GO:0004407,GO:0017136, GO:0046969
SIRT2	sirtuin 2	GO:0017136
SIRT6	sirtuin 6	GO:0017136,GO:0046969

TAL1	T-cell acute lymphocytic leukemia 1	GO:0000118
TBL1X	transducin (beta)-like 1X-linked	GO:0000118
TBL1XR1	transducin (beta)-like 1 X-linked receptor 1	GO:0000118
ZNF217	zinc finger protein 217	GO:0000118
	Histone methylation	
ASH1L	ash1 (absent, small, or homeotic)-like	GO:0018024
ASH2L	ash2 (absent, small, or homeotic)-like	GO:0042800
CARM1 (PRMT4)	coactivator-associated arginine methyltransferase 1	GO:0035642, GO:0042054
CXXC1	CXXC finger protein 1	GO:0042800
DOT1L	DOT1-like, histone H3 methyltransferase	GO:0018024
EED	embryonic ectoderm development	GO:0042054, GO:0035098,
EHMT1	euchromatic histone-lysine N-methyltransferase 1	GO:0046976, GO:0046974, GO:0018024, GO:0006306
EHMT2	euchromatic histone-lysine N-methyltransferase 2	GO:0018024，GO:0046974，GO:0046976, GO:0006306
EZH1	enhancer of zeste homolog 1	GO:0046976 ,GO:0035098
EZH2	enhancer of zeste homolog 2	GO:0042054, GO:0018024, GO:0035098
FBXO11	F-box protein 11	[2]
MEN1	multiple endocrine neoplasia I	GO:0018024
MLL	myeloid/lymphoid or mixed-lineage leukemia	GO:0042800
MLL2	myeloid/lymphoid or mixed-lineage leukemia 2	GO:0018024
MLL3	myeloid/lymphoid or mixed-lineage leukemia 3	GO:0042800
MLL4	myeloid/lymphoid or mixed-lineage leukemia 2	GO:0042800
MLL5	myeloid/lymphoid or mixed-lineage leukemia 5	GO:0042800, GO:0006306
NSD1	nuclear receptor binding SET domain protein 1	GO:0042799, GO:0042054, GO:0046975
PRDM1	PR domain containing 1, with ZNF domain	[18]
PRDM10	PR domain containing 10	[18]
PRDM11	PR domain containing 11	[18]
PRDM12	PR domain containing 12	[18]
PRDM13	PR domain containing 13	[18]
PRDM14	PR domain containing 14	[18]
PRDM15	PR domain containing 15	[18]
PRDM16	PR domain containing 16	[18]
PRDM2	PR domain containing 2, with ZNF domain	GO:0018024
PRDM4	PR domain containing 4	[18]
PRDM5	PR domain containing 5	[18]
PRDM6	PR domain containing 6	GO:0018024
PRDM7	PR domain containing 7	GO:0042800
PRDM8	PR domain containing 8	[18]
PRDM9	PR domain containing 9	GO:0018024
PRMT1	protein arginine methyltransferase 1	GO:0042054, GO:0044020
PRMT2	protein arginine methyltransferase 2	GO:0008469, GO:0042054
PRMT3	protein arginine methyltransferase 3	[2]
PRMT5	protein arginine methyltransferase 5	GO:0008469
PRMT6	protein arginine methyltransferase 6	GO:0042054, GO:0044020, GO:0070612, GO:0070611
PRMT7	protein arginine methyltransferase 7	GO:0008469, GO:0044020
PRMT8	protein arginine methyltransferase 8	GO:0008469
RBBP5	retinoblastoma binding protein 5	GO:0042800
SETD1A	SET domain containing 1A	GO:0042800, GO:0018024
SETD1B	SET domain containing 1B	GO:0042800

SETD2	SET domain containing 2	GO:0018024
SETD3	SET domain containing 3	GO:0046975
SETD7	SET domain containing (lysine methyltransferase) 7	GO:0018024
SETD8	SET domain containing (lysine methyltransferase) 8	GO:0018024
SETDB1	SET domain, bifurcated 1	GO:0018024
SETDB2	SET domain, bifurcated 2	GO:0046974
SETMAR	SET domain and mariner transposase fusion gene	GO:0018024
SMYD2	SET and MYND domain containing 2	GO:0046975
SMYD3	SET and MYND domain containing 3	GO:0018024
SUV39H1	suppressor of variegation 3-9 homolog 1	GO:0042054, GO:0046974, GO:0018024
SUV39H2	suppressor of variegation 3-9 homolog 2	GO:0046974, GO:0018024
SUV420H1	suppressor of variegation 4-20 homolog 1	GO:0042799, GO:0018024
SUV420H2	suppressor of variegation 4-20 homolog 2	GO:0042799
SUZ12	suppressor of zeste 12 homolog	GO:0042054, GO:0035098
WDR5	WD repeat domain 5	GO:0042800
WDR82	WD repeat domain 82	GO:0042800
WHSC1	Wolf-Hirschhorn syndrome candidate 1	GO:0018024
WHSC1L1	Wolf-Hirschhorn syndrome candidate 1-like 1	GO:0018024
	Histone demethylation	
C14orf169	chromosome 14 open reading frame 169	GO:0032453, GO:0051864
JHDM1D	jumonji C domain containing histone demethylase 1 homolog D	GO:0032454, GO:0035575, GO:0051864, GO:0071558
JMJD6	jumonji domain containing 6	GO:0033746, GO:0033749
KDM1A	lysine (K)-specific demethylase 1A	GO:0032452, GO:0032453,GO:0032454, GO:0034648
KDM1B	lysine (K)-specific demethylase 1B	GO:0034648, GO:0034649
KDM2A	lysine (K)-specific demethylase 2A	GO:0051864
KDM2B	lysine (K)-specific demethylase 2B	GO:0032452,GO:0051864,
KDM3A	lysine (K)-specific demethylase 3A	[18]
KDM4A	lysine (K)-specific demethylase 4A	GO:0051864
KDM4C	lysine (K)-specific demethylase 4C	GO:0032454
KDM5B	lysine (K)-specific demethylase 5B	GO:0034647,GO:0034648
KDM5C	lysine (K)-specific demethylase 5C	GO:0032453
KDM5D	lysine (K)-specific demethylase 5D	GO:0032453
KDM8	lysine (K)-specific demethylase 8	GO:0051864
PADI4	peptidyl arginine deiminase, type IV	[18]
PHF2	PHD finger protein 2	GO:0032454
PHF8	PHD finger protein 8	GO:0032452,GO:0032454, GO:0035575,GO:0051864, GO:0071558
	Chromatin remodeling	
ACTL6A	Actin-like 6A	GO:0016514, GO:0031011
ACTL6B	Actin-like 6B	GO:0016514
ACTR5	ARP5 actin-related protein 5 homolog	GO:0031011
ACTR8	ARP8 actin-related protein 8 homolog	GO:0031011
AEBP2	AE binding protein 2	GO:0035098,
ARID1A	AT rich interactive domain 1A (SWI-like)	GO:0016514
ARID1B	AT rich interactive domain 1B (SWI1-like)	GO:0016514
ASF1A	ASF1 anti-silencing function 1 homolog A	GO:0016585
BAZ1B	bromodomain adjacent to zinc finger domain, 1B	GO:0043044, GO:0016585
BMI1	BMI1 polycomb ring finger oncogene	GO:0035102
BPTF	bromodomain PHD finger transcription factor	GO:0016589
C17orf49	chromosome 17 open reading frame 49	GO:0016589
CBX1	chromobox homolog 1	[13]

CBX2	chromobox homolog 2	GO:0035102
CBX4	chromobox homolog 4	GO:0035102
CBX7	chromobox homolog 7	GO:0035102
CBX8	chromobox homolog 8	GO:0035102
CHAF1A	chromatin assembly factor 1, subunit A (p150)	GO:0033186
CHAF1B	chromatin assembly factor 1, subunit B (p60)	GO:0033186
CHD1	chromodomain helicase DNA binding protein 1	[23]
CHD2	chromodomain helicase DNA binding protein 2	[23]
CHD5	chromodomain helicase DNA binding protein 5	[23]
CHD6	chromodomain helicase DNA binding protein 6	[23]
CHD7	chromodomain helicase DNA binding protein 7	[23]
CHD8	chromodomain helicase DNA binding protein 8	GO:0043044
CHD9	chromodomain helicase DNA binding protein 9	[23]
HMGXB4	HMG box domain containing 4	GO:0016589
INO80	INO80 homolog	GO:0031011
INO80B	INO80 complex subunit B	GO:0031011
INO80C	INO80 complex subunit C	GO:0031011
INO80E	INO80 complex subunit E	GO:0031011
JARID2	jumonji, AT rich interactive domain 2	GO:0035098
KIF11	kinesin family member 11	GO:0016585
MAEL	maelstrom homolog	GO:0016585
MCRS1	microspherule protein 1	GO:0031011
MYSM1	Myb-like, SWIRM and MPN domains 1	GO:0016585
NCR1	natural cytotoxicity triggering receptor 1	GO:0016514
NFRKB	nuclear factor related to kappaB binding protein	GO:0031011
PCGF2	polycomb group ring finger 2	GO:0035102
PCGF6	polycomb group ring finger 6	GO:0035102
PHC1	polyhomeotic homolog 1	GO:0035102
PHC2	polyhomeotic homolog 2	GO:0035102
PHC3	polyhomeotic homolog 3	GO:0035102
PHF1	PHD finger protein 1	[5]
RB1	retinoblastoma 1	GO:0016514
RBM10	RNA binding motif protein 10	GO:0016585
RING1	ring finger protein 1	GO:0035102
RNF2	ring finger protein 2	GO:0035102
RSF1	remodeling and spacing factor 1	GO:0031213
RUVBL1	RuvB-like 1	GO:0031011
RUVBL2	RuvB-like 2	GO:0031011
SMARCA1	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 1	GO:0016589, GO:0043044
SMARCA2	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 2	GO:0016514
SMARCA4	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 4	GO:0016514
SMARCA5	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 5	GO:0016589, GO:0031213, GO:0043044
SMARCB1	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily b, member 1	GO:0016514
SMARCC1	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily c, member 1	GO:0016514
SMARCC2	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily c, member 2	GO:0016514
SMARCD1	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily d, member 1	GO:0016514, GO:0016585
SMARCD2	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily d, member 2	GO:0016514

SMARCD3	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily d, member 3	GO:0016514
SMARCE1	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily e, member 1	GO:0016514
SOX9	SRY (sex determining region Y)-box 9	GO:0016585
TFPT	TCF3 (E2A) fusion partner	GO:0031011
UCHL5	ubiquitin carboxyl-terminal hydrolase L5	GO:0031011
YY1	YY1 transcription factor	GO:0031011

Table 2: GO terms and corresponding IDs of human epigenetic genes

Type	GO Term	GO ID
DNA methylation	DNA-methyltransferase activity	GO:0009008, GO:0003886, GO:0051718
	methyl-CpG binding	GO:0008327
	DNA methylation	GO:0006306
	DNA demethylation	GO:0080111
Histone modification	histone acetyltransferase activity	GO:0010484, GO:0010485, GO:0004402
	histone acetyltransferase complex	GO:0000123
	histone deacetylase activity	GO:0017136, GO:0032041, GO:0046969, GO:0046970, GO:0043997
	histone deacetylase complex	GO:0000118
	histone methyltransferase activity	GO:0008469, GO:0018024, GO:0035642, GO:0042054, GO:0042799, GO:0042800, GO:0044020, GO:0046974, GO:0046975, GO:0046976, GO:0070611, GO:0070612
	histone demethylase activity	GO:0004407, GO:0032452, GO:0034648, GO:0071558, GO:0051864, GO:0032453, GO:0032454, GO:0034649, GO:0033746, GO:0034647, GO:0035575, GO:0033749
chromatin remodeling	chromatin remodeling	GO:0043044, GO:0016585
	NuRD complex	GO:0016581
	SWI/SNF complex	GO:0016514
	NURF complex	GO:0016589
	Ino80 complex	GO:0031011
	RSF complex	GO:0031213
	CAF-1 complex	GO:0033186
	PRC1 complex	GO:0035102
	PRC2 complex	GO:0035098

* Results from GeneOntology in February 2012

Table 3. Function descriptions of 12 DD genes and 16 UU genes

Symbol	Function described in UniProt Knowledgebase	Tumor-related function
C14orf169	Histone demethylase that specifically demethylates 'Lys-4' (H3K4me) and 'Lys-36' (H3K36me) of histone H3.	Induction of C14orf169 into NIH3T3 cells conferred growth-promoting activity, while suppression of its expression suppressed growth of cancer cells [29].
PRMT7	Arginine methyltransferase that can both catalyze the formation of omega-N monomethylarginine (MMA) and symmetrical dimethylarginine (sDMA).	Downregulation of PRMT7 was associated with an increased sensitivity of Hela cells to camptothecin and an increase in apoptosis [31].
PRMT3	Methylates (mono and asymmetric dimethylation) the guanidino nitrogens of arginyl residues in some proteins.	N/A
RUVBL1	Possesses single-stranded DNA-stimulated ATPase and ATP-dependent DNA helicase (3' to 5') activity.	Expression of RUVBL1 increased in liver cancer, and depletion of its expression in liver cancer cells led to growth arrest [11].
CBX4	E3 SUMO-protein ligase which facilitates SUMO1 conjugation by UBE2I	N/A
CHD7	Probable transcription regulator	Depletion of CHD7 reduced protein synthesis and cell proliferation [36].
DNMT1	Methylates CpG residues. Preferentially methylates hemimethylated DNA.	Causing silence of tumor-suppressor genes in cancer cells [24]. R educed Dnmt1 expression can inhibit tumor formation in a mouse model [32].
PRMT5	Arginine methyltransferase that can both catalyze the formation of omega-N monomethylarginine (MMA) and symmetrical dimethylarginine (sDMA).	Expression of PRMT5 is elevated in gastric cancer and lymphoma [14,21]. PRMT5 regulates cell growth and proliferation by controlling expression of genes involved in tumor suppression [22].
UCHL5	Protease that specifically cleaves 'Lys-48'-linked polyubiquitin chains.	UCHL5 up-regulate of TGF-β signaling [32] and its expression increases in cervical carcinoma [25]. b-AP15 inhibited the activity of UCHL5 and induced apoptosis of cancer cells [8].

CHD1	ATP-dependent chromatin-remodeling factor which functions as substrate recognition component of the transcription regulatory histone acetylation (HAT) complex SAGA.	Expression of CHD1 reduced in tumors, and depletion of this gene promoted cell invasiveness [12].
PRMT1	Arginine methyltransferase that methylates (mono and asymmetric dimethylation) the guanidino nitrogens of arginyl residues.	PRMT1 expression increased in cancer cells of various tissues and Abrogation of the depletion of this gene suppressed growth of bladder and lung cancer cells [35].
MTA1	May be involved in the regulation of gene expression by covalent modification of histone proteins.	Forced expression of this gene causes inappropriate mammary gland development and tumorigenesis [1].
NCOR2	Transcriptional corepressor of NR4A2/NURR1 and acts through histone deacetylases (HDACs) to keep promoters of NR4A2/NURR1 target genes in a repressed deacetylated state.	NCOR2 was silenced in non-Hodgkin lymphoma, and *In vitro* down-regulation of SMRT induces transformed phenotype to immortalized fibroblasts [28].
KDM4C	Histone demethylase that specifically demethylates 'Lys-9' and 'Lys-36' residues of histone H3.	KDM4C was amplified in various tumors and inhibiting the expression of this gene inhibited cell proliferation[7].
FTO	Dioxygenase that repairs alkylated DNA and RNA by oxidative demethylation.	N/A
KAT5	Catalytic subunit of the NuA4 histone acetyltransferase complex which is involved in transcriptional activation of select genes principally by acetylation of nucleosomal histones H4 and H2A.	KAT5 counteracts Myc-induced lymphomagenesis and LOH of this gene is a frequent event in lymphomas and mammary carcinomas [10].
BPTF	Histone-binding component of NURF (nucleosome-remodeling factor), a complex which catalyzes ATP-dependent nucleosome sliding and facilitates transcription of chromatin.	The BPTF chromosomal region was amplified in various tumors depletion of BPTF inhibited cell proliferation [3].
NCOA2	Transcriptional coactivator for steroid receptors and nuclear receptors.	deletion of NCOA2 in mice predisposes to diethylnitrosamine-induced liver tumorigenesis [19].
PHF15	Component of the HBO1 complex which has a histone H4-specific acetyltransferase activity.	N/A
SMARCA1	Energy-transducing component of NURF (nucleosome-remodeling factor) and CERF (CECR2-containing-remodeling factor) complexes. Both complexes facilitate the perturbation of chromatin structure in an ATP-dependent manner.	Inhibition of SMARCA1 expression cause growth-arrest and death of cancer cells [34].

BMI1	Component of a Polycomb group (PcG) multiprotein PRC1-like complex, a complex class required to maintain the transcriptionally repressive state of many genes.	The Bmi-1 is elevated in many types of cancers, and depletion of this genes causes apoptosis and/or senescence in tumor cells [4].
MGEA5	Possesses hyaluronidase activity. Acetylates 'Lys-8' of histone H4 and 'Lys-14' of histone H3.	N/A
KDM3A	Histone demethylase that specifically demethylates 'Lys-9' of histone H3.	Expression of KDM3A increase in cancer cells of various tissues [6]. Depletion of this gene is sufficient to reduce tumor growth in vivo [15].
ATF7IP	Recruiter that couples transcriptional factors to general transcription apparatus and thereby modulates transcription regulation and chromatin formation.	ATF7IP is frequently overexpressed in cancers of different tissues, and depletion of this genes results in decreased telomerase activity [17].
HDAC5	Responsible for the deacetylation of lysine residues on the N-terminal part of the core histones (H2A, H2B, H3 and H4).	N/A
KDM4A	Histone demethylase that specifically demethylates 'Lys-9' and 'Lys-36' residues of histone H3.	N/A
KDM5B	Histone demethylase that demethylates 'Lys-4' of histone H3.	KDM5B is overexpressed in breast cancer cells [33] , and may promote tumourigenesis by downregulating expression of genes such as BRCA1 and HOXA5 [26].
ING4	Component of the HBO1 complex which has a histone H4-specific acetyltransferase activity, a reduced activity toward histone H3 and is responsible for the bulk of histone H4 acetylation in vivo.	ING4 overexpression diminished colony-forming efficiency, induced apoptosis, and inhibited melanoma cell invasion [16,27].

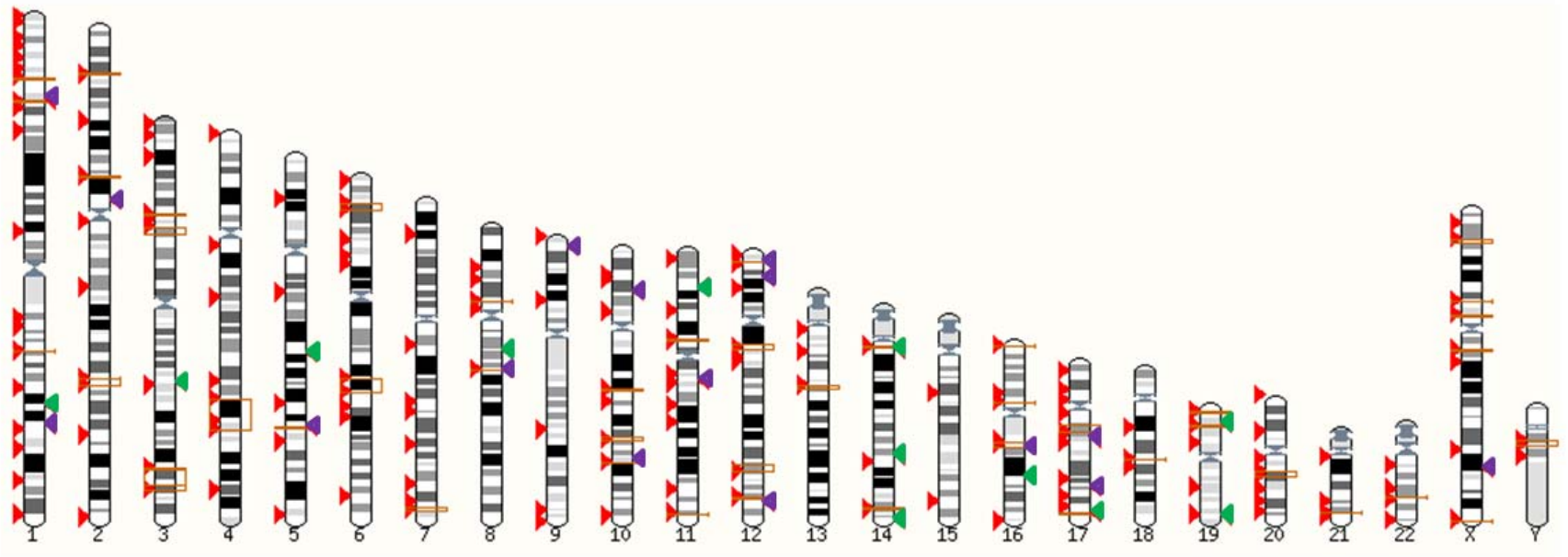


Fig. 1

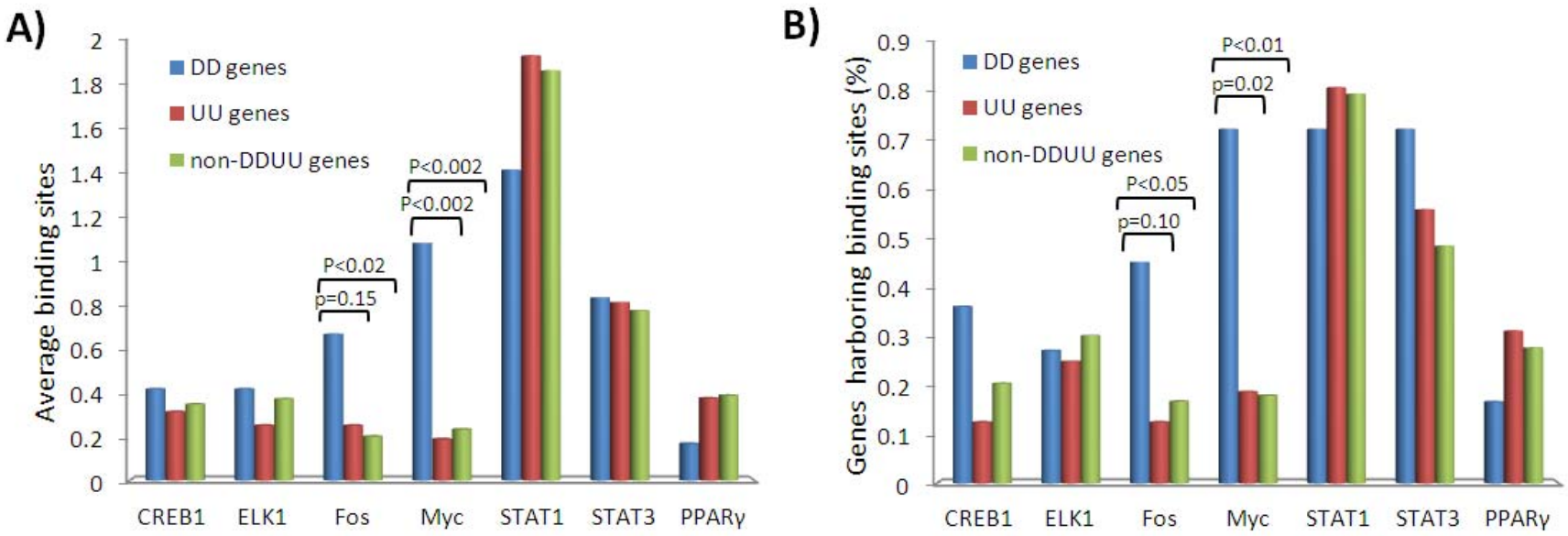
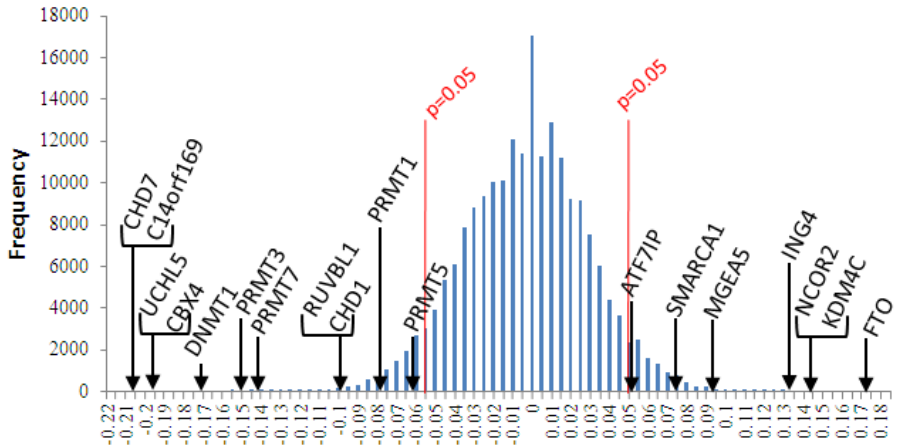

A)
Average binding sites
DD genes
UU genes
non-DDUU genes
P<0.02
p=0.15
P<0.002
P<0.002
CREB1
ELK1
Fos
Myc
STAT1
STAT3
PPARγ
B)
Genes harboring binding sites (%)
DD genes
UU genes
non-DDUU genes
P<0.05
p=0.10
P<0.01
p=0.02
CREB1
ELK1
Fos
Myc
STAT1
STAT3
PPARγ

Fig.2

A)


Frequency
CHD7
C14orf169
UCHL5
CBX4
DNMT1
PRMT3
PRMT7
RUVBL1
CHD1
PRMT1
PRMT5
p=0.05
p=0.05
ATF7IP
SMARCA1
MGEA5
ING4
NCOR2
KDM4C
FTO

B)

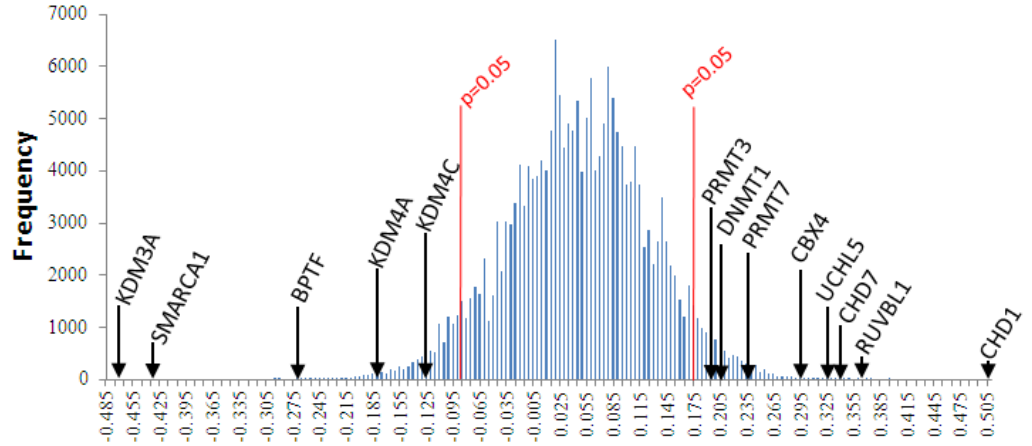

Frequency
KDM3A
SMARCA1
BPTF
KDM4A
KDM4C
p=0.05
p=0.05
PRMT3
DNMT1
PRMT7
CBX4
UCHL5
CHD7
RUVBL1
CHD1

Fig.3

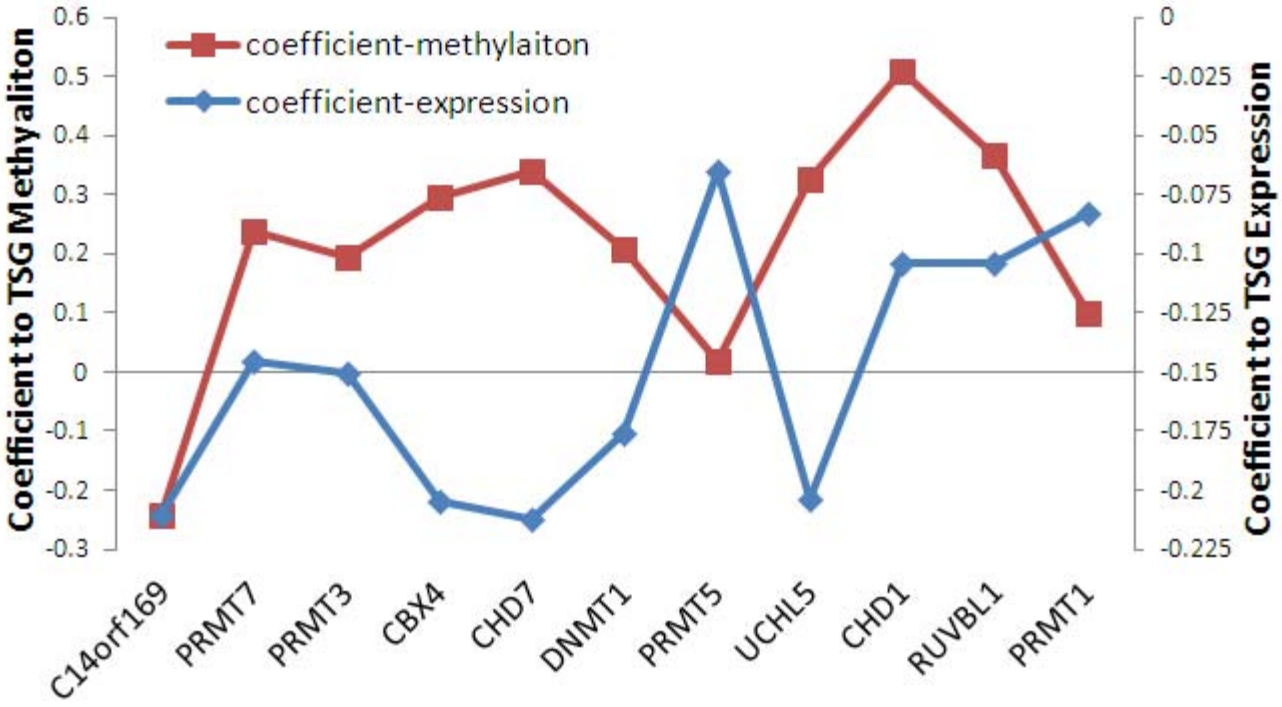

coefficient-methylaiton
coefficient-expression
Coefficient to TSG Methyaliton
Coefficient to TSG Expression
0.6
0.5
0.4
0.3
0.2
0.1
0
-0.1
-0.2
-0.3
0
-0.025
-0.05
-0.075
-0.1
-0.125
-0.15
-0.175
-0.2
-0.225
C14orf169
PRMT7
PRMT3
CBX4
CHD7
DNMT1
PRMT5
UCHL5
CHD1
RUVBL1
PRMT1

Fig. 4

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