Alternative splicing, epigenetic modifications and cancer: A dangerous triangle, or a hopeful one?

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SUPPLEMENTARY MATERIALS

Table S1. Writers, readers and erasers of DNA methylation.

Writers and their functions [1]	**Readers** [2]	**Erasers and their mechanism** [3]
DNMT1	Methyl binding domain (MDB)-containing proteins	Ten-eleven translocation (TET) enzymes
Responsible for *de novo* methylation	MeCP1	TET1
	MeCP2	TET2
DNMT3A	MBD1	TET3
DNMT3B	MBD2	
Use hemimethylated DNA as substrate.	MBD3	Catalyse oxidative removal of methyl
Function: maintenance of methylation in mitotic division	MBD4	group *via* 5- hydroxymethylcytosine
DNMT3L		
DNMT3B3		
No DNA methyl transferase activity; only regulatory roles		

Table S2. Writers, readers and erasers of histone acetylation.

Writers [4–6]	**Readers** [7–11]	**Erasers** [12–14]
GCN5/PCAF family (GNAT) GCN5 (KAT2A), PCAF (KAT2B), HAT1 (KAT1), ELP3 (KAT9), ATF2 *MYST family* MOF/MYST1 (KAT8), MOZ/MYST3 (KAT6A), MORF/MYST4 (KAT6B), HBO1/MYST2 (KAT7), TIP60 (KAT5) *p300/CBP family* CBO (KAT3B), CBP (KAT3A) *SRC family* SRC-1 (KAT13A), ACTR/SRC-3 (KAT13B), TIF-2 /NCOA2(KAT13C), CLOCK (KAT13D) *TRANSCRIPTION CO-ACTIVATORS family* TAF1/TAFII250 (KAT4), FIIIC220/ GTF3C1	**Bromodomain** *BRD family I* PCAF, GCN5L2, FALZ/BPTF, CECR2, BAZ1A *BRD family II* BRD2, BRD3, BRD4, BRDT *BRD family III* EP300, CREBBP, WDR9, PHIP, BRD8B, BAZ1B, BRWD3 *BRD family IV* BRD1, BRD7, BRD9, BRPF1A, BRPF1B, BRPF3, ATAD2, ATAD2B/KIAA1240 *BRD family V* TRIM66, TRIM33, TRIM24/TIF1α, SP100, SP110, SP140, SP140L, LOC93349, BAZ2A, BAZ2B *BRD family VI* MLL, TRIM28 *BRD family VII* ZMYND11, ZMYND8, TAF1, TAF1L, WDR9d1, BRWD3d1, PHIPd1 *BRD family VIII* ASH1L, SMARCA2, SMARCA4, PBRM1/PB1 **Tandem-PHD domain** MOZ (KAT6A), MORF (KAT6B), DPF1 (BAF complex), DPF2 (BAF complex), DPF3 (BAF complex) **YEATS domain** AF9 (YEATS3), YAF9 (YEATS4), YEATS2, ENL (YEATS1)	*CLASS I family* HDAC1, HDAC2, HDAC3, HDAC8 *CLASS IIa family* HDAC4, HDAC5, HDAC7, HDAC9a, HDAC9b *CLASS IIb family* HDAC6, HDAC10 *CLASS IV family* HDAC11 *SIRTUINS* SIRT1-7

Details on writers, readers and erasers can be found at http://weram.biocuckoo.org/

Table S3. Writers, readers and erasers of histone methylation.

Writers [11,13,15]	**Readers** [8,11,13]	**Erasers** [11,13]
K-HMT	**Chromodomain**	**K-HDM**
SET domain	CHD1, HP1, CDY1, PC1/PC2/PC/LHP1, MSL3, MRG15, CBX1-8, MPP8, Tip60,	**FAD-dependent amine oxidase**
SUV39 family	**PHD domain**	*LSD1 family*
SUB39H1, SUV39H2, G9A, GLP, ESET, CLLL8	ING1-5, BPTF, RAG2, TAF3, ICBP90, PYGO, CHD4, UHRF1 *(*ICBP90), DPF3, KDM5A (JARID1A), KDM5C (JARID1C), KDM7D (JMJD1D), KMT2A (MLL1), KDM7B (PHF8), KDM7C (PHF2)	LSD1(KDM1A), LSD2 (KDM1B)
SET1 family	**Tudor domain**	**Fe^{2+} and α-KG dependent dioxygenase**
MLL1, MLL2, SET1A, SET1B, MLL4, MLL3, EZH2, EZH1	JMJD2A, 53BP1, PHF1, PHF19, PHF20, TDRD3	*KDM2 family*
SET2 family	**PWWP domain**	KDM2A, KDM2B
ASH1, NSD1, NSD2, NSD3, HYPB/HIF1	DNMT3A, BRPF1, PDP1, HDGF2, PSIP1 (LEDGF)	*KDM3 family*
RIZ family	**MBT domain**	KDM3A-3C (JMJD1A-1C)
PRDM1/BLIMP, PDRM2/RIZ, PRDM4/PFM1	PHF20L1, SFMBT, L3MBTL1/2, MBTD1	*KDM4 family*
SMYD family	**WDR domain**	KDM4A-4D
SMYD1, SMYD3	ELP2 (STATIP1), EED, WDR5, TBL1X, TBL1XR1, L3MBTL2 (LIN-61)	*KDM5 family*
SUV4-20 family	**14-3-3 domain**	KDM5A-5D (JARID1A-1D)
SUV4-20H1, SUV4-20H2	14-3-3	*KDM6 family*
SET7/9 family	**ZF-CW domain**	KDM6A(UTX), KDM6B(JMJD3), KDM6C(UTY)
SET7, SET9	ZCWPW1	*KDM7 family*
Non-SET domain	**Ankyrin domain**	KDM7A(JMJD1D), KDM7B(PHF8), KDM7C(PHF2)
DOT1L	G9A/GLP	*KDM8 family*
R-HMT		KDM8 (JMJD5)
PRMT Type-I family		**R-HDM**
PRMT1, PRMT2, PRMT3, PRMT4 (CARM1), PRMT6, PRMT8		PAD4/PADI4, JMJD6
PRMT Type-II family		
PRMT5, PRMT9		
PRMT Type-III family		
PRMT7		

Details on writers, readers and erasers can be found at http://weram.biocuckoo.org/

Table S4. Epidrugs approved or under clinical trial.

Inhibitors of DNA methylation		Inhibitors of HDACs		Inhibitors of bromodomains		Inhibitors of PRMTs	
Name	**status**	**Name**	**status**	**name**	**status**	**name**	**status**
Azacitidine	approved	Panobinostat	approved	I-BET762	CT	GSK3326595	CT
Decitabine	approved	Belinostat	approved	Birabresib	CT	AMG 193	CT
Aza-TdCyd	CT	Valproic Acid	approved	CPI-610	CT	JNJ-64619178	CT
		Romidepsin	approved	FT-1101	CT	PF-06939999	CT
		Vorinostat	approved	ZEN-3694	CT	PRT811	CT
		Pracinostat	approved as orphan drug	BMS-986158	CT	IDE397	CT
		Entinostat	CT	OTX-015	CT	PRT543	CT
		Abexinostat	CT	ABBV-075	CT		
		CUDC-101	CT	GS-5829	CT		
		Givinostat	CT	PLX-51107	CT		
		Mocetinostat	CT	TEN-010	CT		

The names of the epidrugs approved or under clinical trials (CT) are given, although some of them were approved for diseases other than cancer. Further details can be obtained from [16,17]. The progress of the clinical trials can be checked at https://www.clinicaltrials.gov/

Table S5. Drugs targeting mRNA splicing, approved or under clinical trials.

Splicing modulators		Drugs targeting enzymes involved in splicing		
Name	**status**	**name**	**status**	**target**
Risdiplam	approved	SM08502	CT	CLKs
Branaplam	approved as orphan drug			
Aclarubicin	CT			

The names of the drugs approved or under clinical trials (CT) are given. CLK stands for CDC2-like kinases. Further details can be obtained from [18–20]. The progress of the clinical trials can be checked at https://www.clinicaltrials.gov/

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