Comprehensive Catalog of Currently Documented Histone Modifications

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SUMMARY

Modern techniques in molecular biology, genomics, and mass spectrometry-based proteomics have identified a large number of novel histone posttranslational modifications (PTMs), many of whose functions are still under intense investigation. Here, we catalog histone PTMs under two classes: first, those whose functions have been fairly well studied and, second, those PTMs that have been more recently identified but whose functions remain unclear. We hope that this will be a useful resource for researchers from all biological or technical backgrounds, aiding in their chromatin and epigenetic pursuits.

Outline

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Histone posttranslational modifications (PTMs) have been linked to a variety of processes, including transcription, DNA replication, and DNA damage (Kouzarides 2007; Murr 2010; for a list of reviews, see Suggested Reviews). The growing list of histone PTMs has exploded in the last several years as a consequence of the considerable advances in available antibody reagents, peptide and protein array technology, and mass spectrometry-based proteomics (Karch et al. 2013). These approaches allow for identification and quantification of histone PTMs from global or more local chromatin states, especially when combined with chromatin immunoprecipitation experiments (Han and Garcia 2013). Here, we attempt to catalog the ever-growing number of histone PTMs that have been studied over the last several years. The tables are broken down into two groups: Section 1 (Tables 1–8) lists the histone PTMs that have been studied more and thus some functional aspects are known concerning the marks; Section 2 (Tables 9–16) lists the histone PTMs that have been detected, but in which rather limited function has been determined. The latter category of histone marks, being in their observed infancy, is very intriguing and represents a large opportunity for the chromatin biology and epigenetics communities to decipher their biological consequences and outcomes in the years to come. Histone acetylation and methylation were first discovered about 50 years ago (Allfrey et al. 1964); however, only in the last decade or so has its physiological function been uncovered. We anticipate that this will serve as a useful resource for those already working in the field, but also as motivation for those newer scientists beginning their research work in this area to continue to push the boundaries of knowledge.

Model organism key

An	Aspergillus nidulans
At	Arabidopsis thaliana
Bt	Bos torus
Ce	Caenorhabditis elegans
Dm	Drosophila melanogaster
Hs	Homo sapiens
Mm	Mus musculus
Nc	Neurospora crassa
Rn	Rattus norvegicus
Sc	Saccharomyces cerevisiae
Sp	Schizosaccharomyces pombe
Tt	Tetrahymena thermophila
Xl	Xenopus laevis

Modification key

ac	acetylation	mal	malonylation
ar1	mono-ADP-ribosylation	mel	monomethylation
bio	biotinylation	me2	dimethylation
but	butyrlyation	me3	trimethylation
cit	citrullination	og	O-GlcNAcylation
cr	crotonylation	oh^*	hydroxylation
for	formylation	ox^*	oxidation
gt*	glutathionylation	ph	phosphorylation
hib	2-hydroxyisobutyrylation	su	SUMOylation
iso	isomerization	ub	ubiquitination

^{*} XYZ modifications are known to occur on histone proteins but have not been included in these tables at individual amino acid residues.

Table heading key

Site A known histone PTM is indicated, based on the Brno nomenclature (Turner 2005), by the numbered amino acid residue

at which it occurs followed by the abbrevation for its chemical modification (see Modification key).

Model Refers to the model organism in which a PTM was characterized.

Enzyme Where known, the histone-modifying enzyme (writer) that transduces a PTM is indicated. Italics specify the valency

of modification that an enzyme can catalyze.

Function The associated biological function of a histone PTM is indicated where known. Reference The key primary references where a PTM and/or its function are described are listed.

1 MORE-STUDIED HISTONE PTMS

The tables in this section list histone modifications with known functions and modifying enzymes, and primary references are indicated wherever possible (up until 2014). Distinct modification states are indicated in italics in the Enzyme column.

Additional modifications with currently unknown function are listed in Section 2. These modifications were obtained from a combination of sources.

The tables that constitute Section 1 have been extended from Appendix 2 in Allis et al. (2007) by Ben Garcia and Yingming Zhao, with additional input from Le Hehuang, Monika Lachner, and Marie-Laure Caparros. That appendix was based on an original setup from Lachner et al. (2003) and significantly extended by Roopsha Sengupta, Mario Richter, and Marie-Laure Caparros and verified by Patrick Trojer.

The histone modifications follow the nomenclature as proposed by Turner (2005).

Table 1. Histone H2A

Site	Model	Enzyme	Function	Reference(s)
K5ac	Hs, Sc	Tip60, p300/CBP, Hat1	Transcriptional activation	Yamamoto and Horikoshi 1997; Kimura and Horikoshi 1998; Verreault et al. 1998
K9bio		HCS	Acetylation and methylation dependent	Stanley et al. 2001; Kothapalli et al. 2005a;
		Biotinidase	Involved in cell proliferation, gene silencing, and cellular response to DNA damage	Chew et al. 2006
K7ac	Sc	Hat1, Esa1	Transcriptional activation	Suka et al. 2001
K13bio		HCS	Acetylation and methylation dependent	Stanley et al. 2001; Kothapalli et al. 2005a;
		Biotinidase	Involved in cell proliferation, gene silencing, and cellular response to DNA damage	Chew et al. 2006
K13ub	Mm	Rnf168	Part of the DNA damage response to double- stranded DNA breaks	Mattiroli et al. 2012; Gatti et al. 2012
K15ub	Mm	Rnf168	Part of the DNA damage response to double- stranded DNA breaks	Mattiroli et al. 2012; Gatti et al. 2012
K63ub	Mm	Rnf8	Part of the DNA damage response to double- stranded DNA breaks	Huen et al. 2007; Mailand et al. 2007
Q105me	Sc, Hs	Nop1, fibrillarin: <i>me1</i>	Ribosomal gene expression	Tessarz et al. 2014
K119ub	Dm, Hs	dRing, RING1B	Polycomb silencing UV damage response	Wang et al. 2004; Kapetanaki et al. 2006
S121ph	Sc	Mec1	DNA damage response	Wyatt et al. 2003; Harvey et al. 2005
(S122ph)	Sp	PIKK	Telomere silencing	Kawashima et al. 2010
		Bub1	Chromosomal stability	
T125ph	Sc	Mec1	DNA damage response	Wyatt et al. 2003
_		PIKK	Telomere silencing	
K126bio	Hs	HCS	Acetylation and methylation dependent	Stanley et al. 2001; Kothapalli et al. 2005a;
		Biotinidase	Involved in cell proliferation, gene silencing, and cellular response to DNA damage.	Chew et al. 2006
K126su	Sc		Transcriptional repression	Nathan et al. 2006
			Blocks histone acetylation and histone ubiquitination	
K127bio	Hs	HCS	Acetylation and methylation dependent	Stanley et al. 2001; Kothapalli et al. 2005a;
		Biotinidase	Involved in cell proliferation, gene silencing, and cellular response to DNA damage	Chew et al. 2006
S128ph	Sc	Mec1	DNA damage response	Downs et al. 2000; Redon et al. 2003;
(S129ph)		PIKK	Telomere silencing	Wyatt et al. 2003; Downs et al. 2004
K130bio	Hs	HCS	Acetylation and methylation dependent	Stanley et al. 2001; Kothapalli et al. 2005a;
		Biotinidase	Involved in cell proliferation, gene silencing, and cellular response to DNA damage	Chew et al. 2006

Additional H2A modifications: K4ac, K21ac, K74me (Pantazis and Bonner 1981; Song et al. 2003; Aihara et al. 2004). HCS, holocarboxylase synthetase; PIKK, phosphatidylinositol 3-kinase-related kinase.

Table 2. Histone H2AX

Site	Model	Enzyme	Function	Reference(s)
K13ub	Mm	Rnf168	Part of the DNA damage response to double- stranded DNA breaks	Mattiroli et al. 2012; Gatti et al. 2012; Panier and Durocher 2013
K15ub	Mm	Rnf168	Part of the DNA damage response to double- stranded DNA breaks	Mattiroli et al. 2012; Gatti et al. 2012; Panier and Durocher 2013
K63ub	Mm	Rnf8	Part of the DNA damage response to double- stranded DNA breaks	Huen et al. 2007; Mailand et al. 2007; Panier and Durocher 2013
S139ph	Hs, Sc, Dm, Xl	ATM DNA-PK ATR	DNA repair M-phase related Also known as γH2AX	Rogakou et al. 1998; Rogakou et al. 1999; Burma et al. 2001; Stiff et al. 2004; Ichijima et al. 2005; Mukherjee et al. 2006; Ward and Chen 2001
Y142ph	Hs, Mm	WSTF	DNA damage	Xiao et al. 2009

ATM, ataxia telangiectasia mutated; PK, protein kinase; ATR, ataxia telangiectasia and Rad3-related; WSTF, Williams-Beuren syndrome transcription factor.

Table 3. Histone H2B

Site	Model	Enzyme	Function	Reference(s)
K5ac	Hs		Transcriptional activation	Puerta et al. 1995; Galasinski et al. 2002
S10ph	Sc	Ste20	Apoptosis	Ahn et al. 2005
S14ph	Hs, Mm	Mst1/krs2 kinase	Apoptosis	Ajiro 2000; Cheung et al. 2003; Odegard
			Somatic hypermutation and class switch recombination	et al. 2005
K16su	Sc		Gene repression	Nathan et al. 2006
K17su	Sc		Gene repression	Nathan et al. 2006
S33ph	Dm	CTK TAF1	Transcriptional activation	Maile et al. 2004
K34ub	Sc	MSL2	Transcriptional activation	Wu et al. 2011
K120ub	Hs	RNF20/40	Cell-cycle progression in concert with SAGA for transcriptional activation through H3 methylation, DNA damage response, meiosis	Robzyk et al. 2000; Sun and Allis 2002; Kao et al. 2004; Zhu et al. 2005
K123ub	Sc	Rad6(E2) Bre1(E3); <i>ub1</i>	Telomeric silencing by lowering histone methylation at H3K4 and H3K79	Emre et al. 2005

Table 4 Histone H3

Site	Model	Enzyme	Function	Reference(s)
R2me	Hs	CARM1; me1, me2a	Gene expression	Chen et al. 1999; Schurter et al. 2001; Greer
	Mm	PRMT5; me1, me2s	•	and Shi 2012
		PRMT6; me1, me2a		
		PRMT7; me1, me2s		
T3ph	Hs	Haspin	Centromere mitotic spindle function	Polioudaki et al. 2004; Dai et al. 2005
	At			
K4ac	Sc	GCN5, RTT109, Sir2, Hst1	Transcription activation at some promoters	Guillemette et al. 2011
K4me	Sc	Set1; <i>me3</i>	rDNA/telomeric silencing (Sc)	Briggs et al. 2001; Roguev et al. 2001; Nagy
	Ce	Set-2; <i>me1</i> −3	Germ cell maintenance	et al. 2002; Bryk et al. 2002; Bernstein
	Ds	Set1; <i>me2/3</i>		et al. 2002; Santos-Rosa et al. 2002; Lee
	Hs	SETD1A; <i>me1−3</i>	Transcriptional activation (All)	and Skalnik 2005; Lee et al. 2007; Xiao
		SETD1B		et al. 2011
	Tt		Transcriptional activation	Strahl et al. 1999
	Ds	Trx	Trithorax activation	Milne et al. 2002; Nakamura et al. 2002;
	Hs	MLL; <i>me1−3</i>	Gene activation	Greer and Shi 2012
		MLL2		

Continued

Table 4. Continued

Site	Model	Enzyme	Function	Reference(s)
	Ds	Trr	Enhancer function	Herz et al. 2013
	Hs	MLL3; <i>me1−3</i>		
		MLL4		
	Ce	Ash-2; <i>me1</i> −3	Germ cell specification	Beisel et al. 2002; Xiao et al. 2011
	Ds	Ash1; me3	Trithorax activation	
	Hs	ASH1L; <i>me1/3</i>	Gene activation	
	Hs	SETD7; me1	Transcriptional activation	Wang et al. 2001a; Nishioka et al. 2002a; Wilson et al. 2002; Zegerman et al. 200
	Hs	SMYD3; <i>me2/3</i>	Transcriptional activation	Hamamoto et al. 2004
	Mm	Meisetz; me3	Meiotic prophase progression	Hayashi et al. 2005
Ր6ph	Hs	РКСВ	Inhibits AR-dependent transcription	Metzger et al. 2010
R8me	Hs	PRMT5; me1, me2s	Transcriptional repression	Pal et al. 2004
(9ac	Sc	SAGA GCN5	Transcriptional activation	Grant et al. 1999
	Hs	SRC1	Nuclear receptor coactivator	Spencer et al. 1997; Schubeler et al. 2000; Vaquero et al. 2004
	Dm		Transcriptional activation	Nowak and Corces 2000
K9me	Sp	Clr4; me1, me2	Centromeric and mating-type	Bannister et al. 2001; Nakayama et al. 200
			silencing	•
	Nc	Dim5; me3	DNA methylation	Tamaru and Selker 2001
	Ce	Met-2; <i>me3</i>	Germ cells	Bessler et al. 2010
		Mes-2; <i>me3</i>		
	Dm	Su(var)3-9; <i>me2/3</i>	Dominant PEV modifier	Czermin et al. 2001; Schotta et al. 2002; Ebert et al. 2004
	At	KRYPTONITE; me2	DNA methylation	Jackson et al. 2002; Jackson et al. 2004
	Mm	Suv39h1; <i>me2/3</i> Suv39h2; <i>me2/3</i>	Pericentric heterochromatin	O'Carroll et al. 2000; Rea et al. 2000; Lachner et al. 2001; Peters et al. 2001
	Hs	SUV39H1; me3	Rb-mediated silencing	Nielsen et al. 2001; Vandel et al. 2001
	Hs, Mm	ESET; me2/me3 (SETDB1)	Transcriptional repression	Schultz et al. 2002; Yang et al. 2002; Dodş et al. 2004; Wang et al. 2004
	Mm, Hs	G9a; me1/me2	Transcriptional repression Imprinting	Tachibana et al. 2001, 2002; Ogawa et al. 2002; Xin et al. 2003
	Hs	EHMT1/GLP; me1/me2	Transcriptional repression	Ogawa et al. 2002; Tachibana et al. 2005
	Hs	PRDM2/RIZ1; me2	Tumor suppression and response to female sex hormones	Kim et al. 2003; Carling et al. 2004
810ph	Sc	Snf1	Transcriptional activation	Lo et al. 2001
	Dm	Jil-1	Transcriptional up-regulation of male X-chromosome	Jin et al. 1999; Wang et al. 2001c
	Hs	Rsk2 Msk1 Msk2	Transcriptional activation of immediate early genes (in concert with H3-K14 acetylation)	Sassone-Corsi et al. 1999; Thomson et al. 1999; Cheung et al. 2000; Clayton et al 2000
	Hs	ΙΚΚα	Transcriptional up-regulation	Anest et al. 2003; Yamamoto et al. 2003
	Sc, Ce	Ip11/AuroraB	Mitotic chromosome condensation	Hendzel et al. 1997; Wei et al. 1999; Hsu et al. 2000
	An	NIMA	Mitotic chromosome condensation	De Souza et al. 2000
	Hs, Ce	Fyn kinase	UVB-induced MAP kinase pathway	He et al. 2005
Γ11ph	Hs	Dlk/ZIP	Mitosis-specific phosphorylation	Preuss et al. 2003
K14ac	Sc, Tt, Mm	Gcn5	Transcriptional activation	Brownell et al. 1996; Kuo et al. 1996
	Hs, Dm	$TAF_{II}230$ $TAF_{II}250$	Transcriptional activation	Mizzen et al. 1996
	Hs	p300	Transcriptional activation	Schiltz et al. 1999
	Hs	PCAF	Transcriptional activation	Schiltz et al. 1999
	Mm	SRC1	Nuclear receptor coactivator	Spencer et al. 1997
R17me	Hs, Mm	CARM1; me1, me2a	Transcriptional activation (in concert with H3-K18/23 acetylation)	Chen et al. 1999; Schurter et al. 2001; Bau et al. 2002; Daujat et al. 2002

 Table 4. Continued

Site	Model	Enzyme	Function	Reference(s)
K18ac	Sc	SAGA	Transcriptional activation	Grant et al. 1999
		Ada		
		GCN5		
	Hs	p300	Transcriptional activation	Schiltz et al. 1999
	Hs	CBP	Transcriptional activation (in concert with H3-R17 methylation)	Daujat et al. 2002
K23ac	Sc	SAGA	Transcriptional activation	Grant et al. 1999
	Hs	CBP	Transcriptional activation (in concert with H3-R17 methylation)	Daujat et al. 2002
R26me	Hs	CARM1; me1, me2a	In vitro methylation site	Chen et al. 1999; Schurter et al. 2001
K27ac	Sc, Dm	CBP, P300, GCN5	Enhancer function, gene expression	Tie et al. 2009; Suka et al. 2001; Creyghton et al. 2010
K27me	Hs, Dm	E(z)/EZH2; me3	Polycomb repression	Cao et al. 2002; Czermin et al. 2002;
			Early B-cell development X-chromosome inactivation	Kuzmichev et al. 2002; Muller et al. 2002; Su et al. 2003
S28ph	Hs	Aurora-B	Mitotic chromosome	Goto et al. 1999; Goto et al. 2002
520pH	113	Autora-D	condensation	Goto et al. 1999, Goto et al. 2002
	Hs	MSK1	UVB-induced phosphorylation	Zhong et al. 2001
K36me	Sc	Set2; me2	Gene repression	Strahl et al. 2002; Kizer et al. 2005; Sun et al. 2005
	Nc	Set2; me2	Transcription activation	Adhvaryu et al. 2005
	Sp	Set2; <i>me2</i>	Transcription elongation	Morris et al. 2005
	Ce	MES-4; me2	Dosage compensation in germline	Bender et al. 2006; Andersen and Horvitz
		MET-1; me3	Meiosis	2007
	Dm	MES4; me3	Transcription elongation	Bell et al. 2007
		SET2; me3		
	Hs, Mm	SETD2; <i>me1−3</i>	Transcription activation	Edmunds et al. 2008
		NSD1-3; <i>me1</i> , <i>me2</i>		Wang et al. 2007
K36ac	Sc, Mm, Hs	GCN5	Promoter mark on active genes	Morris et al. 2007
P38iso	Sc	Fpr4	Gene expression	Nelson et al. 2006
Y41ph	Hs	JAK2	Gene expression	Dawson et al. 2009
R43me	Hs	CARM1, PRMT6; me2a	Transcriptional activation	Casadio et al. 2013
T45ph	Sc, Hs	Cdc7, PKC	DNA replication; apoptosis	Baker et al. 2010; Hurd et al. 2009
K56ac	Sc	SPT10	Transcriptional activation; DNA damage	Xu et al. 2005; Ozdemir et al. 2005; Masumoto et al. 2005
K56me	Hs	G9a; me1	DNA replication	Yu et al. 2012
	Hs	Suv39h; me3	Heterochromatin	Jack et al. 2013
K64ac	Hs/Mm	p300	Nucleosome dynamics and transcription	Di Cerbo et al. 2014
K64me	Mm	те3	Pericentric heterochromatin	Daujat et al. 2009
K79me	Sc, Hs	Dot1/DOT1L;	Telomeric silencing,	Feng et al. 2002; Lacoste et al. 2002; Ng et al.
		me1-3	pachytene checkpoint	2002; van Leeuwen et al. 2002; Greer and
			DNA damage response	Shi 2012
T80ph	Hs		Mitosis	Hammond et al. 2014

Table 5. Histone H3.3

Site	Model	Enzyme	Function	Reference(s)
K4me	Dm	me1, me2, me3	Transcriptional activation	McKittrick et al. 2004
K9me	Dm	me1, me2	Transcriptional repression	McKittrick et al. 2004
K9ac	Dm, Hs		Transcriptional activation	McKittrick et al. 2004; Hake et al. 2006
K14me	Dm	me1, me2	•	McKittrick et al. 2004
K14ac	Dm, Hs		Transcriptional activation	McKittrick et al. 2004; Hake et al. 2006
K18ac	Hs		Transcriptional activation	Hake et al. 2006
K23ac	Hs		Transcriptional activation	Hake et al. 2006
K27me	Dm	me1, me2, me3	Transcriptional repression	McKittrick et al. 2004
S31ph	Mammals		Mitosis-specific phosphorylation	Hake et al. 2005
K36me	Dm, Hs	me1, me2, me3	Transcriptional activation	McKittrick et al. 2004; Hake et al. 2006
K37me	Dm	me1, me2	•	McKittrick et al. 2004
K79me	Dm, Hs	me1, me2	Transcriptional activation	McKittrick et al. 2004; Hake et al. 2006

Table 6. CEN-H3/CENP-A

Site	Model	Enzyme	Function	Reference
G1me3	Hs	RCC1	Mitosis	Bailey et al. 2013
S7ph	Hs		Mitosis	Zeitlin et al. 2001
S16ph	Hs		Chromosome segregation during mitosis	Bailey et al. 2013
S18ph	Hs		Chromosome segregation during mitosis	Bailey et al. 2013

Table 7. Histone H4

Site	Model	Enzyme	Function	Reference(s)
S1ph	Hs, Sc	Casein kinase II	DNA damage response	Ruiz-Carrillo et al. 1975; Cheung et al. 2005; van Attikum and Gasser 2005
R3me	Hs, Sc	PRMT1; me1, me2a PRMT5; me1, me2s PRMT6; me1, me2a PRMT7; me1, me2s	Transcriptional activation	Wang et al. 2001b; Strahl et al. 2001; Greer and Shi 2012
K5ac	Tt, Dm, Hs	Hat1	Histone deposition	Sobel et al. 1995; Parthun et al. 1996; Taplick et al. 1998; Kruhlak et al. 2001
	Sc	Esa1/NuA4	Cell-cycle progression	Smith et al. 1998; Allard et al. 1999; Clarke et al. 1999; Miranda et al. 2006; Bird et al. 2002
	Hs, Mm	ATF2	Sequence-specific transcription factor	Kawasaki et al. 2000a
	Hs	p300	Transcriptional activation	Schiltz et al. 1999; Turner and Fellows 1989
K5me	Hs	Smyd3; me1	Contributes to cancer phenotype	Van Aller et al. 2012
K8ac	Hs, Mm	Y-ATF2	Excluded from Xi	Jeppesen and Turner 1993; Choy et al. 2001;
			Sequence-specific transcription factor	Kruhlak et al. 2001; Kawasaki et al. 2000b
	Hs	PCAF/ p300	Transcriptional activation	Schiltz et al. 1999; Turner and Fellows 1989
K8me	Sc	SET5; me1	Stress response	Green et al. 2012
K12ac	Sc, Hs	Hat1	Excluded from Xi Histone deposition	Jeppesen and Turner 1993; Kleff et al. 1995; Sobel et al. 1995; Parthun et al. 1996; Chang et al. 1997; Kruhlak et al. 2001; Turner and Fellows 1989
	Sc	NuA4	Mitotic and meiotic progression	Choy et al. 2001
K12me	Sc	SET5; me1	Stress response	Green et al. 2012
				Continued



Table 7. Continued

Site	Model	Enzyme	Function	Reference(s)
K12bio	Hs	HCS Biotinidase	Decrease in response to DNA double-strand breaks	Stanley et al. 2001; Kothapalli et al. 2005a,b
K16ac	Mm		Effects on cell proliferation Excluded from Xi Cell-cycle-dependent acetylation	Jeppesen and Turner 1993; Taplick et al. 1998
	Dm	MOF	Transcriptional up-regulation of male X chromosome	Akhtar and Becker 2000; Hsu et al. 2000
	Hs, Mm	ATF2	Sequence-specific transcription factor	Kawasaki et al. 2000a; Turner 2000; Kruhlak et al. 2001; Turner and Fellows 1989; Vaquero et al. 2004
K20me	Mm, Dm	Suv4-20h1; <i>me2</i> , <i>me3</i> Suv4-20h2; <i>me2</i> , <i>me3</i>	Gene silencing	Schotta et al. 2004
	Hs, Dm	SETD8/Pr-SET7; me1	Transcriptional silencing Mitotic condensation	Fang et al. 2002; Nishioka et al. 2002b; Rice et al. 2002
	Dm	Ash1; me2	Trithorax activation in concert with H3K4 and H3K9 methylation	Beisel et al. 2002
K59me	Sc		Silent chromatin formation	Zhang et al. 2003
K59su	Hs	SUMO-1 SUMO-3	Transcriptional repression	Shiio and Eisenman 2003

Table 8. Histone H1

Site	Model	Enzyme	Function	Reference(s)
E2arn	Rn	PARP-1; ar1	Involved in neurotrophic activity	Ogata et al. 1980b; Visochek et al. 2005
T10ph	Hs		Mitosis specific	Chadee et al. 1995; Garcia et al. 2004; Sarg
			Transcriptional activation H1b	et al. 2006
E14arn	Rn	PARP-1; ar1	Involved in neurotrophic activity	Ogata et al. 1980b; Visochek et al. 2005
S17ph	Hs		Interphase specific	Chadee et al. 1995; Garcia et al. 2004; Sarg
			Transcriptional activation H1b	et al. 2006
K26me	Hs	EZH2; me2	Mediates HP1 binding	Kuzmichev et al. 2004; Daujat et al. 2005
S27ph	Hs	EZH2; me2	Blocks HP1 binding	Garcia et al. 2004; Daujat et al. 2005
R54cit	Mm	PADI4	Cellular reprogramming/nucleosome binding	Christophorou et al. 2014
T137ph	Hs		Mitosis specific	Chadee et al. 1995; Garcia et al. 2004; Sarg
			Transcriptional activation H1b	et al. 2006
T154ph	Hs		Mitosis specific	Chadee et al. 1995; Garcia et al. 2004; Sarg
			Transcriptional activation H1b	et al. 2006
S172ph	Hs		Interphase specific	Chadee et al. 1995; Garcia et al. 2004; Sarg
			Transcriptional activation H1b	et al. 2006
S188ph	Hs		Interphase specific	Chadee et al. 1995; Garcia et al. 2004; Sarg
			Transcriptional activation H1b	et al. 2006
K213ar	Rn	PARP-1; ar1	Involved in neurotrophic activity	Ogata et al. 1980b; Visochek et al. 2005

2 LESS-STUDIED HISTONE PTMS

Methods key

The method by which novel histone modifications have been identified is indicated by the following abbreviations:

antibody Ab autoradiography Au mass spectrometry MS

These tables reflect modification sites that have been detected, but where no function has been assigned.

Table 9. Histone H2A^{a,b}

Site	Model	Method	Reference(s)
S1ph	Mm	Au	Pantazis and Bonner 1981
R3me3	Mm	MS	Tweedie-Cullen et al. 2012
K5hib	Mm	MS	Dai et al. 2014
K9me1; me2; suc; hib	Hs; Mm; Hs; Hs	MS	Tan et al. 2011; Tweedie-Cullen et al. 2012; Xie et al. 2012; Dai et al. 2014
R11me1, me2	Hs	MS	Waldmann et al. 2011
K13me1, ac; suc	Bt; Sc	MS	Zhang et al. 2003; Xie et al. 2012
K15ac	Bt	MS	Zhang et al. 2003
K21suc	Sc	MS	Xie et al. 2012
R29me1, me2	Hs	MS/Ab	Waldmann et al. 2011
K36ac, suc; for; hib; cr	Hs/Dm; Hs/Mm; Mm; Hs/Mm	MS	Xie et al. 2012; Wisniewski et al. 2008; Dai et al. 2014; Tan et al. 2011
Y39oh	Hs	MS	Tan et al. 2011
R42me1	Hs; Hs	MS/Ab	Tan et al. 2011
R71me1	Mm	MS	Tweedie-Cullen et al. 2012
K74ac, me1; hib	Mm; Mm	MS	Tweedie-Cullen et al. 2012; Dai et al. 2014
K75me1; hib	Bt; Mm	MS	Zhang et al. 2003; Dai et al. 2014
R77me1	Bt	MS	Zhang et al. 2003
T79ac	Mm	MS	Tweedie-Cullen et al. 2012
R88me1	Hs	MS	Tan et al. 2011
K95cr, but, pr, me1, me2; for; ub; suc; hib	Mm; Hs/Mm; Mm; Hs; Hs/Mm	MS	Tweedie-Cullen et al. 2012; Wisniewski et al. 2008; Tweedie- Cullen et al. 2009; Xie et al. 2012; Dai et al. 2014
K99me1; me2	Mm; Mm	MS	Tweedie-Cullen et al. 2012; Tweedie-Cullen et al. 2009
T101og	Hs	MS/Ab	Sakabe et al. 2010
K118for, me1, cr; for; ub, me2; hib	Hs/Mm; Hs/Mm; Mm; Mm	MS	Tan et al. 2011; Wisniewski et al. 2008; Tweedie-Cullen et al. 2009; Dai et al. 2014
K119cr; mal	Hs; Sc	MS	Tan et al. 2011; Xie et al. 2012
T120ph	Dm	Ab	Aihara et al. 2004
K125me1, cr; me2, pr; ub	Hs; Mm; Mm	MS	Tan et al. 2011; Tweedie-Cullen et al. 2012; Tweedie-Cullen et al. 2009
K127ac	Mm	MS	Tweedie-Cullen et al. 2012
K129ac	Mm	MS	Tweedie-Cullen et al. 2012

^aCarbonylation of H2A has been detected in Rn indirectly by Sharma et al. (2006).

Table 10. Histone H2AX

Site	Model	Method	Reference
K118ub	Mm	MS	Tweedie-Cullen et al. 2009
K119ub	Mm	MS	Tweedie-Cullen et al. 2009

^b5-Hydroxylation of lysine residues has been reported for canonical histones (H2A, H2B, H3, and H4) by Unoki et al. (2013).

Table 11. Histone H2A.Z

Site	Model	Method	Reference(s)
K4ac; me1	Hs; Hs/Mm	MS; MS/Ab	Tweedie-Cullen et al. 2009; Binda et al. 2013
K7ac; me1	Hs; Hs/Mm	MS; MS/Ab	Bonenfant et al. 2006; Binda et al. 2013
K11ac	Hs	MS	Bonenfant et al. 2006
K13ac	Mm	MS	Tweedie-Cullen et al. 2009
K120ub	Mm	MS	Ku et al. 2012
K121ub	Mm	MS	Ku et al. 2012
K125ub	Mm	MS	Ku et al. 2012

Table 12. Histone macroH2A

Site	Model	Method	Reference(s)
K17me1	Hs	MS	Chu et al. 2006
K115ub	Hs	MS	Ogawa et al. 2005; Chu et al. 2006
K122me2	Hs	MS	Chu et al. 2006
T128ph	Hs	MS/Ab	Chu et al. 2006; Bernstein et al. 2008
K238me1	Hs	MS	Chu et al. 2006
K238me2	Hs	MS	Chu et al. 2006

Table 13. Histone H2B

Site	Model	Method	Reference(s)
E2arn	Rn	Au	Ogata et al. 1980a
K5me1; cr; for; hib; suc	Bt; Hs; Hs/Mm; Hs/	MS	Zhang et al. 2003; Tan et al. 2011; Wisniewski et al. 2008;
	Mm; Hs		Dai et al. 2014; Weinert et al. 2013
S6ph	Mm	MS	Tweedie-Cullen et al. 2009
K11ac; cr	Sc; Hs/Mm	MS	Jiang et al. 2007; Tan et al. 2011
K12me1, cr; me3; hib	Hs; Mm; Mm	MS	Tan et al. 2011; Tweedie-Cullen et al. 2012; Dai et al. 2014
K15ac; me1, cr	Hs	MS	Tan et al. 2011
K16ac; cr	Sc; Hs	MS	Jiang et al. 2007; Tan et al. 2011
T19ac	Mm	MS	Tweedie-Cullen et al. 2012
K20me1, cr; hib	Hs; Mm	MS	Tan et al. 2011; Dai et al. 2014
K21but	Sc	MS	Zhang et al. 2009
K23me1, cr; me2; hib	Hs; Bt; Mm	MS	Tan et al. 2011; Zhang et al. 2003; Dai et al. 2014
K24hib	Mm	MS	Dai et al. 2014
K34for; cr; suc; me1; hib	Hs/Mm; Hs/Mm; Sc/ Hs; Mm; Mm	MS	Wisniewski et al. 2008; Tan et al. 2011; Xie et al. 2012; Tweedie-Cullen et al. 2012; Dai et al. 2014
S360g	Hs	MS/Ab	Sakabe et al. 2010
K37me1	Sc	MS	Zhang et al. 2009
E38me2	Sc	MS	Zhang et al. 2009
Y37oh	Hs	MS	Tan et al. 2011
K43me1; for; hib; suc	Bt; Hs/Mm; Mm; Hs	MS	Zhang et al. 2003; Wisniewski et al. 2008; Dai et al. 2014; Weinert et al. 2013
K46for; suc; hib	Hs/Mm; Sc/Dm; Hs/ Mm	MS	Wisniewski et al. 2008; Xie et al. 2012; Dai et al. 2014
K57me1; ac; hib	Hs; Mm; Mm	MS	Tan et al. 2011; Tweedie-Cullen et al. 2012; Dai et al. 2014
E64me2	Sc	MS	Zhang et al. 2009
S76ph	Mm	MS	Tweedie-Cullen et al. 2009
K79me1	Hs	MS	Tan et al. 2011
K85ac; me1; suc; hib	Bt; Hs; Hs; Hs/Mm	MS	Zhang et al. 2003; Tan et al. 2011; Weinert et al. 2013; Dai et al. 2014
S88ph	Mm	MS	Tweedie-Cullen et al. 2009
T89ph	Mm	MS	Tweedie-Cullen et al. 2009
S92ph	Mm	MS	Tweedie-Cullen et al. 2009
K99me1	Hs	MS	Tan et al. 2011
K108for; cr; ub, ac; hib; suc	Hs/Mm; Mm; Mm; Hs/Mm; Mm	MS	Wisniewski et al. 2008; Tweedie-Cullen et al. 2012; Tweedie-Cullen et al. 2009; Dai et al. 2014; Park et al. 2013
S113ph	Mm	MS	Tweedie-Cullen et al. 2009
K116for, me1; suc, mal; ac; hib; cr	Hs; Hs/Dm; Mm; Hs/ Mm; Mm	MS	Tan et al. 2011; Xie et al. 2012; Tweedie-Cullen et al. 2012; Dai et al. 2014; Montellier et al. 2013
K120for; suc; ac, ub; hib	Hs; Hs/Dm/Mm; Mm; Hs/Mm	MS	Tan et al. 2011; Xie et al. 2012; Tweedie-Cullen et al. 2009; Dai et al. 2014
K125ac	Mm	MS	Tweedie-Cullen et al. 2012

Also, 5-hydroxylation of lysine residues has been reported (Unoki et al. 2013).

Table 14. Histone H3

Site	Model	Method	Reference(s)
K4cr; hib; ac	Hs/Mm; Mm; Hs	MS	Tan et al. 2011; Dai et al. 2014; Garcia et al. 2007
T6ac	Tt	MS	Britton et al. 2013
K9cr; hib	Hs/Mm; Mm	MS	Tan et al. 2011; Dai et al. 2014
S10ac; og	Sc/Mm/Hs	MS; Ab; Ab	Britton et al. 2013; Zhang et al. 2011
K14suc; but; hib	Hs; Sc; Mm	MS	Xie et al. 2012; Zhang et al. 2009; Dai et al. 2014
K18cr; for; me1; hib	Hs/Mm; Hs/Mm; Mm; Mm	MS	Tan et al. 2011; Wisniewski et al. 2008; Garcia et al. 2005; Dai et al. 2014
T22ac	Sc/Dm/Hs	MS	Britton et al. 2013
K23cr; for; pr; hib; suc	Hs/Mm; Hs/Mm; Sc; Hs/Mm; Mm	MS	Tan et al. 2011; Wisniewski et al. 2008; Zhang et al. 2009; Dai et al. 2014; Park et al. 2013
K27cr; but; hib; suc	Hs/Mm; Sc; Mm; Mm	MS	Tan et al. 2011; Zhang et al. 2009; Dai et al. 2014; Park et al. 2013
S28ac	Mm	MS	Britton et al. 2013
T32og	Hs	MS	Fong et al. 2012
K36hib	Mm	MS	Dai et al. 2014
R52me1	Sc/Bt	MS	Hyland et al. 2005
R53me1	Sc/Bt	MS	Hyland et al. 2005
Y54ac	Tet	MS	Britton et al. 2013
K56cr, for; suc, mal; pr; ub; hib	Hs/Mm; Dm/Mm/ Hs; Sc; Mm; Hs/Mm	MS	Tan et al. 2011; Xie et al. 2012; Zhang et al. 2009; Tweedie-Cullen et al. 2009; Dai et al. 2014
E59me2	Sc	MS	Zhang et al. 2009
R63me1	Hs/Mm	MS	Tan et al. 2011
K64for; hib; ac, me1	Hs/Mm; Mm; Sc, Hs	MS	Wisniewski et al. 2008; Dai et al. 2014; Garcia et al. 2007
K79suc; for; cr; ub; hib; ac	Sc/Dm/Mm/Hs; Hs/ Mm; Mm; Mm; Hs/ Mm; Hs	MS	Xie et al. 2012; Wisniewski et al. 2008; Tweedie-Cullen et al. 2012; Tweedie-Cullen et al. 2009; Dai et al. 2014; Garcia et al. 2007
T80ac	Mm	MS	Tweedie-Cullen et al. 2012
R83me1, me2	Mm	MS	Tweedie-Cullen et al. 2012
S86ph	Mm	MS	Tweedie-Cullen et al. 2012
T107ph	Mm	MS	Tweedie-Cullen et al. 2012
C110gt	Hs/Mm	Indirect chemical labeling	Garcia-Gimenez et al. 2013
K115ac; but	Sc/Bt; Mm	MS	Hyland et al. 2005; Tweedie-Cullen et al. 2012
T118ph	Sc/Bt	MS	Hyland et al. 2005
R128me1	Hs/Mm	MS	Tan et al. 2011
K122suc; for; me2; hib; cr	Hs; Hs/Mm; Mm; Hs/ Mm; Mm	MS	Tan et al. 2011; Wisniewski et al. 2008; Tweedie-Cullen et al. 2009; Dai et al. 2014; Montellier et al. 2013
K134me1	Mm	MS	Tweedie-Cullen et al. 2012

Also, 5-hydroxylation of lysine residues has been reported (Unoki et al. 2013).

Table 15. Histone H4

Site	Model	Method	Reference(s)
R3me3	Mm	MS	Tweedie-Cullen et al. 2012
K5cr; me3; pr, but; hib	Mm/Hs; Mm; Hs; Mm	MS	Tan et al. 2011; Tweedie-Cullen et al. 2012; Chen et al. 2007; Dai et al. 2014
K8cr; pr, but; hib	Mm/Hs; Hs; Mm	MS; MS; MS/Ab	Tan et al. 2011; Chen et al. 2007; Dai et al. 2014
K12cr; for; suc; pr, but; hib	Mm/Hs; Hs; Hs; Mm	MS	Tan et al. 2011; Wisniewski et al. 2008; Xie et al. 2012; Chen et al. 2007; Dai et al. 2014
K16cr, me1; pr; pr, but; hib	Mm/Hs; Mm; Hs; Mm	MS	Tan et al. 2011; Tweedie-Cullen et al. 2012; Chen et al. 2007; Dai et al. 2014
R17me1, me2	Mm	MS	Tweedie-Cullen et al. 2012
R17me1, me2, me3	Mm	MS	Tweedie-Cullen et al. 2012
K20ac	Sc	MS	Garcia et al. 2007

Continued

Table 15. Continued

Site	Model	Method	Reference(s)
K31for; suc; hib; me1; pr	Hs; Sc/Dm/Mm/Hs; Hs/Mm; Hs/Mm/ Sc; Hs	MS	Tan et al. 2011; Xie et al. 2012; Dai et al. 2014; Garcia et al. 2007; Chen et al. 2007
R23me3	Mm	MS	Tweedie-Cullen et al. 2012
R35me1	Hs	MS	Tan et al. 2011
K44pr; hib	Hs; Mm	MS	Chen et al. 2007; Dai et al. 2014
S47og; ph	Hs; Sc/Bt	MS/Ab; MS	Sakabe et al. 2010; Hyland et al. 2005
Y51oh	Hs	MS	Tan et al. 2011
R55me1	Hs	MS	Tan et al. 2011
K59me1, for; hib	Hs; Mm/Hs; Mm	MS	Tan et al. 2011; Wisniewski et al. 2008; Dai et al. 2014
R67me1	Hs	MS	Tan et al. 2011
K77me1; suc; for; hib; ac; pr; cr	Hs; Sc/Dm/Mm/Hs; Mm/Hs; Hs/Mm; Sc/Bt; Hs; Mm	MS	Tan et al. 2011; Xie et al. 2012; Wisniewski et al. 2008; Dai et al. 2014; Hyland et al. 2005; Chen et al. 2007; Montellier et al. 2013
K79for; suc, ac; hib; pr	Hs; Dm/Mm; Mm; Hs/Mm; Hs	MS	Wisniewski et al. 2008; Xie et al. 2012; Tweedie-Cullen et al. 2012; Dai et al. 2014; Chen et al. 2007
Y88ox; ph	Hs; Mm	MS	Tan et al. 2011; Tweedie-Cullen et al. 2009
K91ac; for; suc; cr; hib; pr	Hs; Hs; Dm/Mm/Hs; Mm; Hs/Mm; Hs	MS	Tan et al. 2011; Wisniewski et al. 2008; Xie et al. 2012; Tweedie-Cullen et al. 2012; Dai et al. 2014; Chen et al. 2007
R92me1	Sc/Bt	MS	Hyland et al. 2005

Also, 5-hydroxylation of lysine residues has been reported (Unoki et al. 2013).

Table 16. Histone H1

Site	Model	Method	Reference(s)
S1ph	Hs	MS	Garcia et al. 2004
E2arn	Rn	Au	Ogata et al. 1980b
T3ph	Hs	MS	Garcia et al. 2004
K12me1	Hs	MS	Lu et al. 2009
E14arn	Rn	Au	Ogata et al. 1980b
K16ac; me1, me2; for	Hs/Mm;	MS	Wisniewski et al. 2007
	Hs/Mm		Wisniewski et al. 2008
T17ph	Hs	MS	Garcia et al. 2004
K21ac; me1	Hs; Mm	MS	Wisniewski et al. 2007; Tweedie-Cullen et al. 2012
K22hib	Mm	MS	Dai et al. 2014
K25hib	Mm	MS	Dai et al. 2014
K26hib	Mm	MS	Dai et al. 2014
S30ph	Hs	MS	Garcia et al. 2004
K33ac; me2, for; cr; ub; hib	Hs; Mm; Hs/Mm; Mm; Mm	MS	Wisniewski et al. 2007; Tweedie-Cullen et al. 2012; Tan et al. 2011; Tweedie-Cullen et al. 2009
S35ph; ac	Hs; Mm	MS	Garcia et al. 2004; Tweedie-Cullen et al. 2012
K45ac,ub; hib; for; suc	Hs; Hs; Hs/Mm; Mm	MS	Wisniewski et al. 2007; Dai et al. 2014; Wisniewski et al. 2008; Park et al. 2013
K48ac	Hs	MS	Wisniewski et al. 2007
S50ac	Mm	MS	Tweedie-Cullen et al. 2012
K51ac; me1; hib	Hs; Mm; Hs/Mm	MS	Wisniewski et al. 2007; Tweedie-Cullen et al. 2012; Dai et al. 2014
K54me1	Hs	MS	Tan et al. 2011
K62ac; for; hib; suc	Hs; Hs/Mm; Hs/Mm; Hs	MS	Garcia et al. 2004; Wisniewski et al. 2008; Dai et al. 2014; Weinert et al. 2013
K63ac; me1; for; cr; hib	Hs; Hs; Hs/Mm; Hs/ Mm; Hs	MS	Wisniewski et al. 2007; Lu et al. 2009; Wisniewski et al. 2008; Tan et al. 2011; Dai et al. 2014
K64ac	Hs	MS	Tan et al. 2011
K66for	Hs/Mm	MS	Wisniewski et al. 2008
	•		Continued

Continued



Table 16. Continued

Site	Model	Method	Reference(s)
-			
S72ph Y73oh	Hs Hs	MS MS	Garcia et al. 2004 Tan et al. 2011
K74for; hib		MS	
K80hib	Hs/Mm; Mm	MS	Wisniewski et al. 2008; Dai et al. 2014
K81me1	Mm Hs	MS	Dai et al. 2014 Lu et al. 2009
K83for		MS	
	Hs		Tan et al. 2011
K84for; cr; hib	Hs/Mm; Hs/Mm; Hs/ Mm	MS	Wisniewski et al. 2008; Tan et al. 2011; Dai et al. 2014
K85ac	Hs	MS	Wisniewski et al. 2007
S87ph ^a	Hs	MS	Garcia et al. 2004
K87for ^a	Hs	MS	Wisniewski et al. 2007
K89ac, for; cr; suc; hib	Hs; Hs; Mm; Hs	MS	Wisniewski et al. 2007; Tan et al. 2011; Park et al. 2013; Dai et al. 2014
K92me1	Hs	MS	Tan et al. 2011
K96ac; me1; me2; for; cr;	Hs; Hs; Mm; Hs/Mm;	MS	Wisniewski et al. 2007; Lu et al. 2009; Tweedie-Cullen et al.
hib; suc	Hs; Hs/Mm; Mm		2012; Wisniewski et al. 2008; Tan et al. 2011; Dai et al. 2014; Park et al. 2013
K101me1	Hs	MS	Lu et al. 2009
K105me1; suc	Hs; Mm	MS	Lu et al. 2009; Park et al. 2013
K107me1	Hs	MS	Lu et al. 2009
K109me2; for; hib	Mm; Hs/Mm; Mm	MS	Tweedie-Cullen et al. 2012; Wisniewski et al. 2008; Dai et al. 2014
S112ac	Mm	MS	Tweedie-Cullen et al. 2012
K118me1	Hs	MS	Lu et al. 2009
K120hib; suc	Mm; Mm	MS	Dai et al. 2014; Park et al. 2013
K128hib	Mm	MS	Dai et al. 2014
K131me1	Hs	MS	Tan et al. 2011
K135hib	Mm	MS	Dai et al. 2014
K140for	Hs/Mm	MS	Wisniewski et al. 2008
T145ph	Hs	MS	Garcia et al. 2004
T146ph	Hs	MS	Garcia et al. 2004
K147me1; hib	Hs; Mm	MS	Lu et al. 2009; Dai et al. 2014
K150me1	Hs	MS	Tan et al. 2011
K158cr; hib	Hs/Mm; Mm	MS	Tan et al. 2011; Dai et al. 2014
K159for	Hs/Mm	MS	Wisniewski et al. 2008
T164ph	Hs	MS	Wisniewski et al. 2007
K167cr; hib	Hs; Mm	MS	Tan et al. 2011; Dai et al. 2014
T179ph	Hs	MS	Garcia et al. 2004
K187me1	Hs	MS/Ab	Weiss et al. 2010
K201me1	Hs	MS	Tan et al. 2011
K212hib	Mm	MS	Dai et al. 2014
K226me1	Hs	MS	Tan et al. 2011

Pham (2000) found an enzyme that ubiquitinates histone H1

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