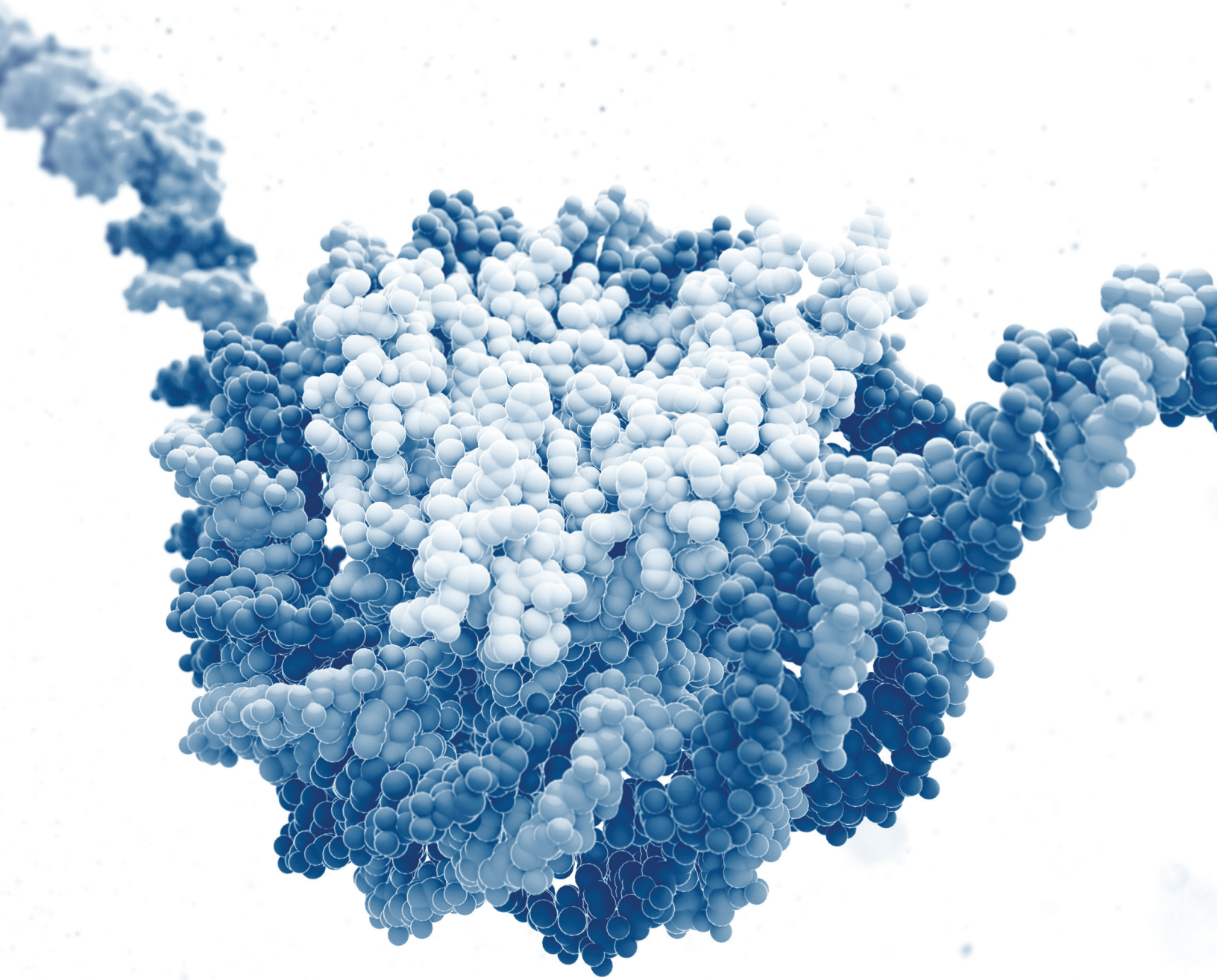
GUIDE

Histone Modification

Inhibition Strategies & Research Tools



Cayman CHEMICAL

Histone modification is an epigenetic mechanism that enables fine-tuning of gene expression by altering chromatin structure and the accessibility of DNA for transcription. The tails of histone proteins can be post-translationally modified by processes including methylation and acetylation. Histone modifications are regulated by proteins called “writers” that add modifications, “erasers” that remove them, and “readers” that recognize modified histone residues and recruit effectors and co-regulators. Mutation or dysregulation of these proteins alters normal gene expression and has been found in a variety of diseases.

Numerous chemical tools have been developed to study the function of histone modifying proteins and their roles in physiological and pathological states. It is important to understand the differences in chemical modulation strategies in order to choose the most appropriate one for your application.

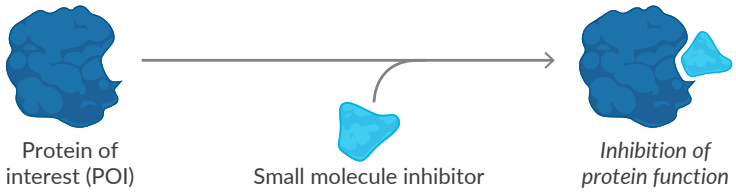
Use this guide to learn about writers, erasers, and readers of two major forms of histone modification, methylation and acetylation, and determine the best chemical modulation strategy for your experiments.

Contents

Chemical Modulation Strategies

Chemical modulation of protein targets is a powerful tool for elucidating protein function in physiological and disease states. Two major chemical modulation strategies are inhibition by small molecule inhibitors and targeted protein degradation by proteolysis-targeting chimeras (PROTACs). It is important to determine the strategy best suited to your target and application.

Small Molecule Inhibitors



Small molecule inhibitors alter protein function by binding to specific protein domains such as catalytic or allosteric sites. They can inhibit certain functions while preserving others. This is important to consider when choosing an inhibition strategy, as many epigenetic proteins have both catalytic and non-catalytic functions.

Chemical Probes

Small molecule inhibitors that meet certain quality criteria can be classified as chemical probes. A chemical probe is a well-characterized small molecule with a defined mechanism of action that potently and selectively modulates the activity of a target protein.

The ideal probe is...

- ✓ **Potent**: IC_{50} or K_d <100 nM *in vitro*
- ✓ **Selective**: >30-fold selectivity for the target over proteins in the same family
- ✓ **Active in cells**: significant on-target cellular activity at <1 µM

It is also important to consider stability, solubility, cell permeability (for intracellular targets), and concentration-dependent effects. The probe should have minimal or no off-target effects. To strengthen the probe set, include an orthogonal control (a probe for the same target with a different chemotype than the primary probe) and at least one negative control (an inactive analog of the primary probe).

Explore our Guide to Choosing & Using Chemical Probes at **www.caymanchem.com/chemicalprobes**

The Structural Genomics Consortium (SGC) is a leader in the development of epigenetic chemical probes and evaluation of probes donated by pharmaceutical companies and academic laboratories.

SGC chemical probes and donated probes are indicated throughout this guide with this color ■

Challenges of Small Molecule Inhibitors and Chemical Probes

- ✓ Isoform selectivity is difficult to achieve
- ✓ Acquired/mutation-driven drug resistance

Epigenetics Screening Library (96-Well)

Item No. 11076

Contains more than 140 small molecule inhibitors of epigenetic writers, erasers, and readers

SGC Epigenetic Probe Set ■

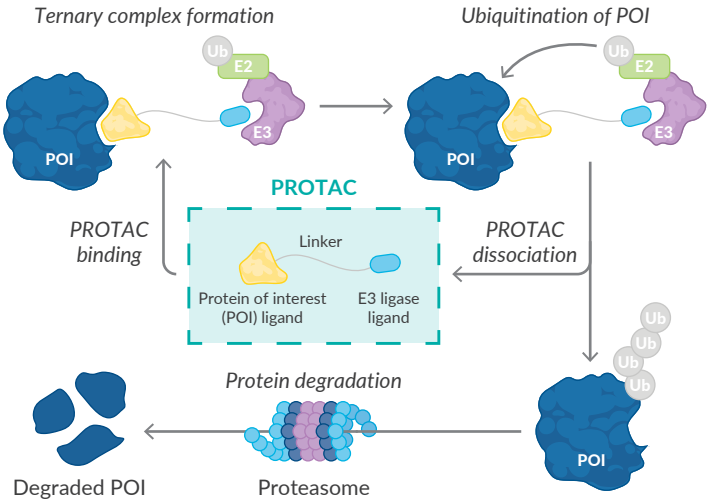
Item No. 17748

Contains more than 65 epigenetic probes from the SGC that inhibit epigenetic writers, erasers, and readers

PROTACs

PROTACs facilitate targeted protein degradation. They are heterobifunctional molecules consisting of two distinct ligands joined by a linker. Typically, the first ligand binds the protein of interest (POI) and the second binds to an E3 ubiquitin ligase that promotes ubiquitination and subsequent proteasomal degradation of the POI.

- By facilitating degradation of the entire target protein, PROTACs eliminate all functions of the protein, both catalytic and non-catalytic.
- PROTACs can achieve improved selectivity compared to small molecule inhibitors.
- PROTACs are less likely to develop acquired drug resistance compared to small molecule inhibitors.
- Unlike small molecule inhibitors, PROTACs do not need to bind to functional sites on target proteins to exert their activity. Instead, they only need to bind to an accessible surface on the target protein.



PROTACs are indicated throughout this guide with this color ■

Challenges of PROTACs

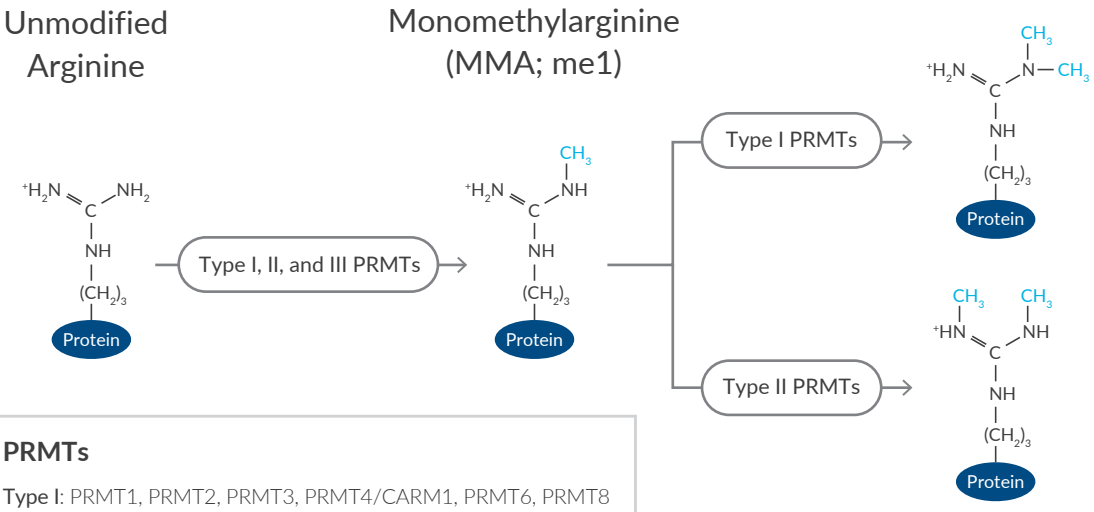
The relatively high molecular weight of PROTACs can present challenges including:

✓ Low solubility ✓ Reduced oral bioavailability ✓ Poor cell permeability

Histone Methylation

Histone Arginine Methylation - Writers

Arginine residues on proteins are subject to methylation by protein arginine methyltransferases (PRMTs). PRMTs can methylate transcription factors, coactivators and co-repressors, signal receptors, and histones. Whether histone arginine methylation activates or represses transcription depends on the specific residue and type of methylation.



PRMTs

Type I: PRMT1, PRMT2, PRMT3, PRMT4/CARM1, PRMT6, PRMT8

Type II: PRMT5, PRMT9 **Type III**: PRMT7

PRMT Inhibitors

Type I Inhibitors

Item No.	Product Name	Target(s)
19160	EPZ020411	PRMT6
29954	EZM2302	PRMT4
19121	Furamidine (hydrochloride)	PRMT1
34886	GSK3368715 (hydrochloride)	Type I PRMTs
18361 ■	MS023 (hydrochloride)	Type I PRMTs
18348 ■	MS049 (hydrochloride)	PRMT4 and PRMT6

Item No.	Product Name	Target(s)
33712 ■	SGC6870	PRMT6
17017 ■	SGC707 *	PRMT3
17718	TC-E 5003	PRMT1
20256 ■	TP-064	PRMT4
18122	UNC2327	PRMT3

** Negative control also available*

Type II & III Inhibitors

Item No.	Product Name	Target(s)
29476	DS-437	PRMT5 and PRMT7
17285	EPZ015666	PRMT5
27305	GSK3326595	PRMT5
18354 ■	GSK591	PRMT5

Item No.	Product Name	Target(s)
29231	JNJ-64619178	PRMT5
21596 ■	LLY-283	PRMT5
25325 ■	SGC3027 †	PRMT7

† Prodrug form

View all PRMT inhibitors at **www.caymanchem.com**

Histone Lysine Methylation

■ *Chemical Probe,* ■ *PROTAC*

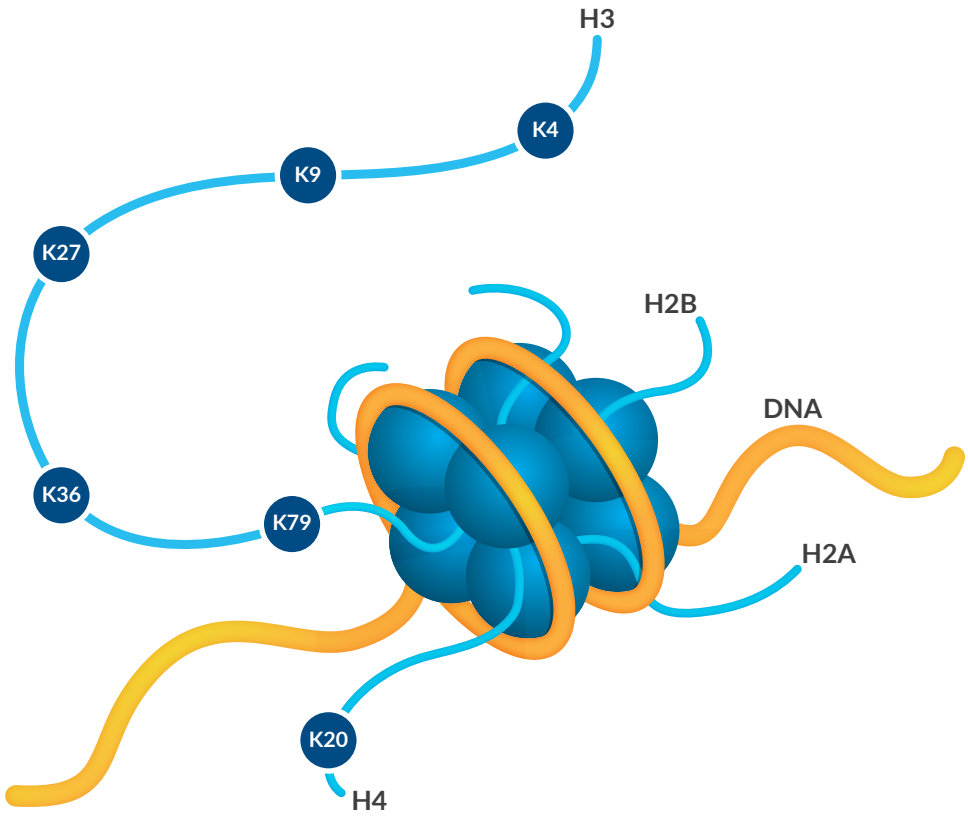
Methylation of lysines on histones can either activate or repress gene transcription, depending on the site of methylation and number of methyl groups added. The most well-studied histone lysine methylation sites are on histone H3 at lysine 4 (H3K4), lysine 9 (H3K9), lysine 27 (H3K27), lysine 36 (H3K36), and lysine 79 (H3K79), as well as on histone H4 at lysine 20 (H4K20).

Writers

Lysine methyltransferases (KMTs) add methyl groups to lysine residues, creating mono-, di-, and trimethylated derivatives (me1, me2, and me3, respectively). Several histone KMTs, including enhancer of zeste homolog 2 (EZH2), DOT1L, and G9a, are overexpressed in various cancers and are promising therapeutic targets. However, many KMTs that methylate histone lysine residues also methylate lysines on non-histone proteins, which should be considered when exploring the use of KMT inhibitors or degraders as therapeutic agents.

Notable Histone KMTs

MLL1-4, SETD1A, SETD1B, SET7/9, SMYD2	K4
G9a, GLP, SUV39H1, SUV39H2, SETDB1	K9
EZH1, EZH2	K27
NSD1-3, ASH1L, SETD2, SMYD2	K36
DOT1L	K79
SET8, SUV420H1, SUV420H2	K20

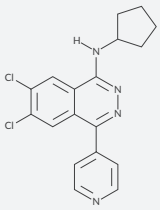


Histone H4 KMTs

A-196 ■

Item No. 18317

A selective inhibitor of SUV420H1 and SUV420H2



SET8 Inhibitors & Assay Kit

Item No.	Product Name
16614	Ryuvidine
16400	UNC0379
700350	SET8 Methyltransferase Inhibitor Screening Assay Kit

Histone H3 KMTs

SET7/9 Inhibitor & Assay Kit

Item No.	Product Name
14678	(R)-PFI-2 (hydrochloride) *
700270	SET7/9 Methyltransferase Inhibitor Screening Assay Kit

** Negative control also available*

G9a & G9a-like protein (GLP) Inhibitors

Item No.	Product Name	Target(s)
16081	A-366	G9a
13124	BIX01294 (hydrochloride hydrate)	G9a
25948	CM-272	G9a, GLP, and DNA methyltransferases
13631	UNC0224	G9a
10734	UNC0638	G9a, GLP
14604	UNC0642	G9a

View all G9a and GLP inhibitors at www.caymanchem.com

SMYD2 Inhibitors

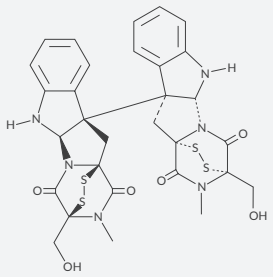
Item No.	Product Name
16875	AZ 505
16441	LLY-507 ‡
29174	(R)-BAY-598
18238	(S)-BAY-598

‡ Multiple off-targets (SGC)

Chaetocin

Item No. 13156

A fungal mycotoxin and inhibitor of Lys9-specific KMTs



EZH1 & EZH2

EZH1 and EZH2 can both function as the catalytic subunit in polycomb repressive complex 2 (PRC2) to methylate H3K27. Along with catalytic inhibition or degradation of EZH1/2, PRC2 can be inhibited through disruption of its interaction with H3K27me3 (see page 9).

EZH2 Inhibitors & PROTAC

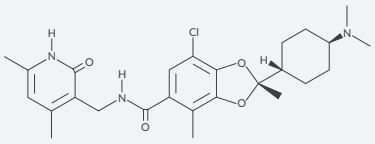
Item No.	Product Name
13828	3-Deazaneplanocin A
16174	EPZ6438
15415	GSK126
14094	GSK343
35466	MS1943
14621	UNC1999

View all EZH2 inhibitors at www.caymanchem.com

Valemetostat

Item No. 31674

A dual EZH1 and EZH2 Inhibitor



NSD2 Inhibitor & Non-PROTAC Degrader

PTD2 (trifluoroacetate salt)

Item No. 38842

A peptide inhibitor of NSD2

UNC8153 (trifluoroacetate salt)

Item No. 38932

A non-PROTAC degrader of NSD2

DOT1L Inhibitors

Item No.	Product Name
36456	DOT1L-IN-4
16173	EPZ004777 (formate)
16175	EPZ5676
13967	SGC0946

View all histone methyltransferase inhibitors at **www.caymanchem.com**

Erasers

Lysine demethylases (KDMs) remove methyl groups from methylated lysines. The KDM1 family removes mono- and dimethylation marks from lysines, while the KDM2-8 families contain a Jumonji C (JmjC) domain and remove mono-, di-, and trimethylation marks. Overexpression of specific KDMs has been observed in a variety of cancer types.

KDM1 Family

LSD1 (KDM1A) and LSD2 (KDM1B) both demethylate H3K4me1/me2. LSD1 can also demethylate H3K9me1/me2.

KDM	Synonym(s)
KDM1A	LSD1
KDM1B	LSD2

KDM2 Family

KDM2A (JHDM1A) and KDM2B (JHDM1B) both demethylate H3K36me1/me2. KDM2B can also demethylate H3K4me3.

KDM	Synonym(s)
KDM2A	JHDM1A
KDM2B	JHDM1B

KDM3 Family

KDM3 (JMJD1, JHDM2) family members specifically demethylate H3K9me1/me2.

KDM	Synonym(s)
KDM3A	JMJD1A, JHDM2A
KDM3B	JMJD1B, JHDM2B
KDM3C	JMJD1C, JHDM2C

KDM4 Family

The KDM4 (JMJD2, JHDM3) family members demethylate H3K9me2/me3, with several also able to demethylate H3K36me2/me3.

KDM	Synonym(s)
KDM4A	JMJD2A, JHDM3A
KDM4B	JMJD2B, JHDM3B
KDM4C	JMJD2C, JHDM3C
KDM4D	JMJD2D, JHDM3D
KDM4E	JMJD2E, KDM4DL

KDM5 Family

The KDM5 (JARID1) family members demethylate H3K4me2/me3.

KDM	Synonym(s)
KDM5A	JARID1A
KDM5B	JARID1B
KDM5C	JARID1C
KDM5D	JARID1D

KDM6 Family

KDM6 family members demethylate H3K27me2/me3, however UTY has miminal activity compared to JMJD3 and UTX.

KDM	Synonym(s)
KDM6A	UTX
KDM6B	JMJD3
KDM6C	UTY

KDM7 Family

KDM7 family members have different roles in the demethylation of H3K9me1/me2, H3K27me1/me2, and/or H4K20me1.

KDM	Synonym(s)
KDM7A	JHDM1D
KDM7B	PHF8, JHDM1F
KDM7C	PHF2, JHDM1E

KDM8 Family

KDM8 (JMJD5) has been shown to demethylate H3K36me2.

KDM	Synonym(s)
KDM8	JMJD5

View all histone lysine demethylase inhibitors at www.caymanchem.com

KDM1A (LSD1) Inhibitors & Assay Kit

Item No.	Product Name
19403	GSK2879552
16439 ■	GSK-LSD1 (hydrochloride)
19136	ORY-1001
15487	SP-2509
700120	LSD1 Inhibitor Screening Assay Kit

View all LSD1 inhibitors at www.caymanchem.com

KDM4 (JMJD2) Family Inhibitors

Item No.	Product Name	Target(s)
37431	KDM4D-IN-1	JMJD2D
17472	ML-324	JMJD2E
18478	NCGC00244536	JMJD2B
13944	N-Oxalylglycine	JMJD2A, JMJD2C, and JMJD2E
33922	Prohexadione	JMJD2A

KDM5 (JARID1) Family Inhibitors

Item No.	Product Name	Target(s)
22127	CPI-455	JARID1A-D
19286	Esculetin	JARID1B
42103	GSK467	JARID1B
41542	JQKD82 (hydrochloride) †	JARID1A
36817	KDM5-C70	JARID1B
16272	PBIT	JARID1A-D

† Prodrug form

KDM6 Family Inhibitors

Item No.	Product Name	Target(s)
12054 ■	GSK-J1 (sodium salt) *	JMJD3 and UTX
12073 ■	GSK-J4 (hydrochloride) *, †	JMJD3 and UTX

** Negative control also available, † Prodrug form*

Multi- & Pan-Jumonji Inhibitors

Item No.	Product Name	Target(s)
70602	Caffeic Acid	JMJD2C and UTX
12033	Daminozide	KDM2A, KDM7A, and PHF8
11572 ■	IOX1	2-oxoglutarate oxygenases, including JMJD2A, JMJD2C, JMJD2E, KDM3A, JARID1C, and JMJD3
15338	JIB-04	Pan-Jumonji (JARID1A, JMJD2A, JMJD2B, JMJD2C, JMJD2E, and JMJD3)
11091	Methylstat (hydrate) †	JMJD2A, JMJD2C, JMJD2E, JMJD3, and PHF8
40120	PFI-90	KDM3B, JMJD2B, JARID1A, and JMJD3
17717	TC-E 5002	KDM2A, KDM7A, and PHF8

† Prodrug form

Readers

■ *Chemical Probe,* ■ *PROTAC*

Methylated lysine and arginine residues can be recognized by proteins possessing a variety of reader domains. Methylated lysines can be read by numerous domain types, including Tudor, malignant brain tumor (MBT), plant homeodomain (PHD), WD40, proline-tryptophan-tryptophan-proline (PWWP), and chromodomains. Methylated arginines are primarily read by Tudor domains but can also be recognized by a subset of PHD and WD40 domains.

Chromodomains

Chromodomains specifically bind to trimethylated lysine residues. The chromodomain-containing chromobox (CBX) proteins CBX2, CBX4, CBX6, CBX7, and CBX8 function as components of polycomb repressive complex 1 (PRC1).

CBX7 Inhibitors

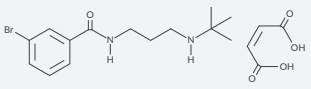
Item No.	Product Name
17533	MS37452
19237	UNC3866

Tudor Domains

Tudor domains can exist as single domains or in tandem repeating units and recognize methylated arginine or lysine residues. Notably, individual Tudor domains can recognize either methylated arginine or lysine, but not both. The methylated lysine reader p53-binding protein 1 (53BP1) possesses tandem Tudor domains.

UNC2170 (maleate)

Item No. 17374



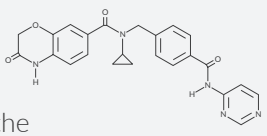
An inhibitor of 53BP1 that binds to the tandem Tudor domains

PWWP Domains

PWWP domains recognize methylated lysine residues and are found in proteins including the nuclear SET domain-containing protein (NSD) family of lysine methyltransferases.

UNC6934 ■

Item No. 28814



A chemical probe and inhibitor of the NSD2-H3K36me2 nucleosome interaction

(Negative control also available)
(See page 6 for NSD2 catalytic inhibitor and degrader)

MBT Domains

MBT domain-containing proteins, including L3MBTL1 and L3MBTL3, recognize methylated lysine residues.

MBT Domain Inhibitors

Item No.	Product Name	Target(s)
13968 ■	UNC1215 *	L3MBTL3
10875	UNC669	L3MBTL1
27302	UNC926	L3MBTL1, L3MBTL3, and L3MBTL4

** Negative control also available*

WD40 Repeat Domains

WD40 repeat domain-containing proteins often function within multiprotein complexes, such as in the case of EED, which is an essential subunit of polycomb repressive complex 2 (PRC2). The methyltransferase activity of PRC2 can be inhibited through disruption of EED binding to H3K27me3.

EED Binding Inhibitors

Item No.	Product Name
20257 ■	A-395 (hydrochloride)
22031	EED226
29316	MAK-683

WD repeat domain 5 (WDR5) can act as part of a core complex with ASH2L, DPY30, and fellow WD40 repeat-containing protein RBBP5 that associates with and stimulates the activity of the SET1/MLL family of H3K4 methyltransferases. Interaction with WDR5 is especially important for the catalytic activity of MLL1.

WDR5 Inhibitors & PROTAC

Item No.	Product Name	Description
41325 ■ ■	Homer	A PROTAC that drives WDR5 degradation
17699	MM-102	An inhibitor of WDR5/MLL interactions
16095 ■	OICR-9429	A chemical probe for WDR5
13945	WDR5-0103	An inhibitor of WDR5 peptide binding

Histone Acetylation

■ *Chemical Probe,* ■ *PROTAC*

Acetylation of lysine residues on histone proteins neutralizes the positive charge of the lysine residue. Acetylated lysine residues are associated with chromatin relaxation and transcriptional activation. Histone acetylation is also associated with the DNA damage response.

Writers

Histone acetyltransferases (HATs) acetylate lysine residues on histone proteins. Major HAT families include the GCN5-related N-acetyltransferase (GNAT), CREB-binding protein (CBP)/p300, and MYST families.

GCN5 & PCAF

GCN5 and PCAF belong to the GNAT family. Each can function as the catalytic HAT subunit in the SAGA and ATAC complexes to acetylate multiple lysines on histones H3 and H4.

GCN5 & PCAF HAT Activity Inhibitors

Item No.	Product Name	Target(s)
12095	Butyrolactone 3	GCN5
10974	CAY10669	PCAF
12086	CPTH2 (hydrochloride)	GCN5
19828	CPTH6 (hydrobromide)	GCN5 and PCAF

HAT Inhibitor Screening Assay Kit
Item No. 10006515
A fast, fluorescence-based method for evaluating PCAF HAT inhibitors

CBP/p300 Family

CBP and p300 are HATs comprising the CBP/p300 family. They can acetylate lysines on multiple histones but are most noted for their acetylation of H3K18 and H3K27.

CBP/p300 HAT Activity Inhibitors

Item No.	Product Name	Target(s)
24119 ■	A-485	p300/CBP
10549	C646	p300
19835	HAT Inhibitor II	p300
17778	L002	p300

GCN5, PCAF, CBP, and p300 also possess bromodomains that recognize acetylated lysine residues and provide additional targets for small molecule inhibitors.

See page 14 for bromodomain inhibitors.

MYST Family

KAT6A (MOZ), KAT6B (MORF), KAT7 (HBO1), KAT8 (MOF), and KAT5 (TIP60) belong to the MYST family of HATs. MYST family HATs associate with several multi-protein complexes to acetylate lysines on multiple histones and regulate transcription.

MYST Family Inhibitors

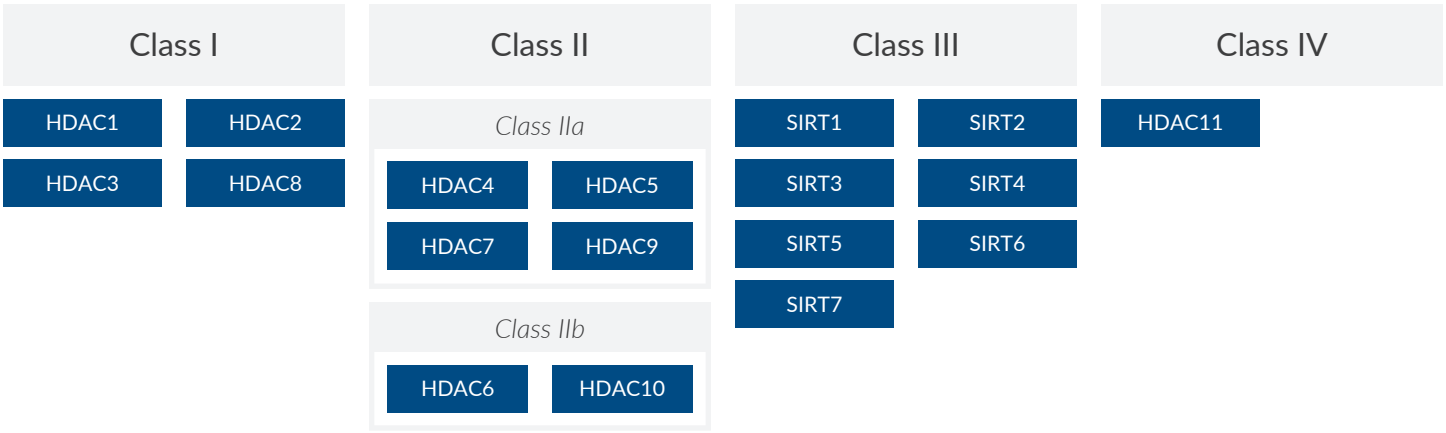
Item No.	Product Name	Target(s)
38977	KAT8 Inhibitor 19	KAT8
22135	MG149	KAT5 and KAT8
27686	MOZ-IN-2	KAT6A
27402	MOZ-IN-3	KAT6A and KAT6B

Item No.	Product Name	Target(s)
37778	PF-9363	KAT6A and KAT6B
30509 ■	WM-1119	KAT6A
40296	WM-3835	KAT6A and KAT7

View all HAT inhibitors at **www.caymanchem.com**

Erasers

Histone deacetylases (HDACs) remove negatively charged acetyl groups from acetylated lysine residues on histones, resulting in more condensed, compacted chromatin and transcriptional repression. Classes I, II, and IV consist of the Zn^{2+}-dependent HDACs (HDAC1-11), whereas class III consists of NAD^{+}-dependent sirtuins (SIRT1-7). Several formulations containing HDAC inhibitors have been FDA-approved for the treatment of T cell lymphoma, multiple myeloma, and Duchenne muscular dystrophy (DMD).



Class I Inhibitors

Item No.	Product Name	Target(s)
13284	MS-275	HDAC1 and HDAC3
10444	PCI 34051	HDAC8
16917	RGFP966	HDAC3
17130	Romidepsin	Class I HDACs
13033	Valproic Acid (sodium salt)	Class I HDACs

Class II Inhibitors

Item No.	Product Name	Target(s)
21531	ACY-1215	HDAC6
26173	ACY-241	HDAC6
14969	LMK 235	HDAC4 and HDAC5
16265	MC 1568	Class IIa HDACs
16874	Nexturastat A	HDAC6
23242	TMP-195	Class IIa HDACs
17738	TMP269	Class IIa HDACs
15785	Tubastatin A	HDAC6

Class IV Inhibitor

Item No.	Product Name	Target(s)
41360	SIS17	HDAC11

Class III Activators & Inhibitors

SIRT Activators

Item No.	Product Name	Target(s)
20209	BML-278	SIRT1, SIRT2, and SIRT3
35528	MDL 800	SIRT6
10011020	SRT 1720 (hydrochloride)	SIRT1
28380	SRT 2104	SIRT1
70675	*trans*-Resveratrol	SIRT1

View all SIRT activators at www.caymanchem.com

SIRT Inhibitors

Item No.	Product Name	Target(s)
10009798	(±)-EX-527	SIRT1
29660	3-TYP	SIRT3
13145	AGK2 *	SIRT2
11127	Nicotinamide	SIRT1
29052	OSS-128167	SIRT6
18116	SirReal2	SIRT2
10523	Sirtinol	SIRT1 and SIRT2
13085	Tenovin-1	SIRT1 and SIRT2

** Negative control also available*
View all SIRT inhibitors at www.caymanchem.com

Multi-Class & Pan-HDAC Inhibitors

Item No.	Product Name	Description
34084	Belinostat	Inhibitor of class I HDACs (IC_{50}s = 0.04, 0.13, 0.03, and 0.22 µM for HDAC1, -2, -3, and -8, respectively) and class II HDACs (IC_{50}s = 0.12, 0.08, 0.07, and 0.13 µM for HDAC4, -6, -7, and -9, respectively)
11045	ITF 2357	An inhibitor of class I and class II HDACs (EC_{50}s = 28, 56, 21, 52, 27, and 163 nM for HDAC1, -2, -3, -4, -6, and -7, respectively, in a fluorometric assay)
18287	Mocetinostat	A orally available HDAC inhibitor that selectively targets HDAC1 and -2 (IC_{50}s = 0.15 and 0.29 µM, respectively) and less potently inhibits HDAC3 and -11 (IC_{50}s = 1.66 and 0.59 µM, respectively)
13280	Panobinostat	A pan-HDAC inhibitor (K_is = 0.6-31 nM for HDAC1-11)
10009929	SAHA	An HDAC inhibitor that inhibits class I, II, and IV HDACs at 50-200 nM
13121	Sodium Butyrate	A short-chain fatty acid and HDAC inhibitor
10496	Sulforaphane	An inhibitor of class I and II HDAC activity that also potently induces chemopreventative enzymes *via* Keap1-Nrf2 signaling and antioxidant response element-driven gene expression
89730	Trichostatin A	A potent, reversible inhibitor of class I, II, and IV HDACs

View all HDAC inhibitors at **www.caymanchem.com**

HDAC/SIRT Activity & Inhibitor Screening Assays

HDAC Assay Kits

Item No.	Product Name
600150	HDAC Cell-Based Activity Assay Kit
10011563	HDAC Fluorometric Activity Assay Kit
10011564	HDAC1 Inhibitor Screening Assay Kit
700230	HDAC8 Inhibitor Screening Assay Kit

SIRT Assay Kits

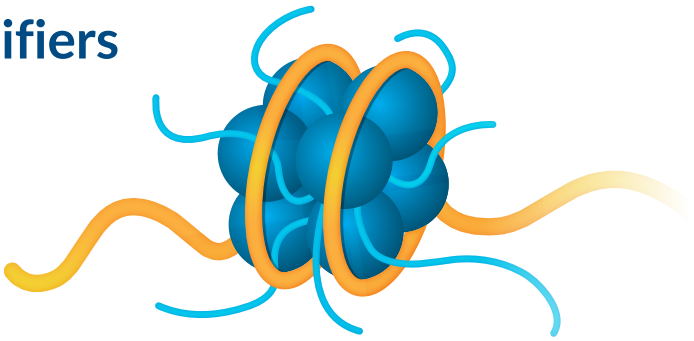
Item No.	Product Name
10010401	SIRT1 Direct Fluorescent Screening Assay Kit
10010991	SIRT1 FRET-Based Screening Assay Kit
700280	SIRT2 Direct Fluorescent Screening Assay Kit
10011566	SIRT3 Direct Fluorescent Screening Assay Kit

Histone Proteins & Their Modifiers

Cayman offers high-quality histone proteins, as well as writers, erasers, and readers of histone methylation and acetylation.

Our proteins can be used for a variety of applications, including enzyme activity assays, Western blot, and ELISA.

Browse epigenetic proteins at www.caymanchem.com



For custom protein and peptide production, visit **www.caymanchem.com/proteinproduction**

Readers

■ *Chemical Probe,* ■ *PROTAC*

Acetylated lysines can be recognized by proteins containing bromodomains, tandem plant homeodomains (PHDs), or YEATS domains. Bromodomain-containing proteins are the best-studied acetylated lysine readers and have roles in a variety of cellular processes.

BET Family Proteins

The bromodomain and extra terminal domain (BET) family is the most extensively characterized family of bromodomain-containing proteins. This family consists of BRD2, BRD3, BRD4, and testis-specific BRDT and is involved in the regulation of transcription. BET proteins possess two highly conserved tandem bromodomains, BD1 and BD2, which bind to acetylated lysines, followed by an extraterminal (ET) domain that facilitates transcriptional cofactor recruitment.

Pan-BET Inhibitors

Item No.	Product Name
11187 ■	(+)-JQ1 *
11181	I-BET151
10676	I-BET762
15947	OTX015

** Negative control also available*

BRD4 PROTACs

Item No.	Product Name
36626 ■	dBET57
35385 ■	dBET6
21622 ■	MZ1

View all BET family PROTACs at www.caymanchem.com

BET Family Inhibitor Screening Assays

Item No.	Product Name
600520	BRD4 bromodomain 1 TR-FRET Assay Kit
600650	BRDT bromodomain 1 TR-FRET Assay Kit

BD1-Selective Inhibitor

Item No.	Product Name
41280 ■	GSK778

BD2-Selective Inhibitors

Item No.	Product Name
30470	ABBV-744
36139 ■	GSK620
42057 ■	GSK973
31766	iBET-BD2
16424	RVX-208
38777	RVX-297

Bivalent BD1/BD2 Inhibitor

Item No.	Product Name
20864	AZD 5153

Bromodomain-Containing Proteins in SWI/SNF Complexes

SWI/SNF chromatin remodeling complexes contain several bromodomain-containing proteins. The bromodomain of the core subunit, SMARCA2 (BRM) or SMARCA4 (BRG1), facilitates histone binding. Additional bromodomain-containing subunits include BRD7, BRD9, and PBRM1 (PB1).

Inhibitors & PROTACs

Item No.	Product Name	Target(s)
36612 ■	ACBI1	SMARCA2, SMARCA4, and PBRM1
17749 ■	I-BRD9	BRD9
17661 ■	LP99	BRD7 and BRD9
15267 ■	PFI-3	SMARCA2, SMARCA4, and PBRM1
33567 ■	SGC-SMARCA-BRDVIII	SMARCA2, SMARCA4, and PBRM1
41454 ■	VZ 185	BRD7 and BRD9

Bromodomain-Containing HATs

■ *Chemical Probe,* ■ *PROTAC*

As discussed on page 10, several histone acetyltransferases, including GCN5, PCAF, CBP, and p300, possess bromodomains in addition to their catalytic HAT domains. The transcription factor IID (TFIID) subunits TAF1 and TAF1L also contain HAT domains and bromodomains.

Bromodomain Inhibitors

Item No.	Product Name	Target(s)
34546	CCS-1477	CBP/p300 bromodomains
20224	CeMMEC13	TAF1 bromodomain 2
36450	GNE-781	CBP/p300 bromodomains
23421 ■	GSK4027	PCAF and GCN5 bromodomains
14468 ■	I-CBP112 (hydrochloride)	CBP/p300 bromodomains
21288 ■	L-Moses (hydrochloride)	PCAF bromodomain
14469 ■	SGC-CBP30	CBP/p300 bromodomains
17123	UMB-32	BRD4, TAF1, and TAF1L bromodomains

Bromodomain Inhibitor Screening Assays

Item No.	Product Name
600850	CBP bromodomain TR-FRET Assay Kit
600870	TAF1 bromodomain 1 TR-FRET Assay Kit
600930	TAF1 bromodomains 1 and 2 TR-FRET Assay Kit

Additional Bromodomain-Containing Proteins

Cayman also offers inhibitors and chemical probes to study other bromodomain-containing proteins with a variety of biological functions.

Bromodomain Inhibitors

Item No.	Product Name	Target(s)
19777 ■	BAY-299	BRD1 (BRPF2) and TAF1
23422 ■	BAY-850	ATAD2
17448 ■	BAZ2-ICR	BAZ2A/B
14119 ■	Bromosporine	Bromodomains
14120 ■	GSK2801	BAZ2A/B
17662 ■	NI-57	BRPF1B, BRD1 (BRPF2), and BRPF3
41164 ■	NVS-BPTF-1	BPTF
18316 ■	NVS-CECR2-1	CECR2
17663 ■	PFI-4	BRPF1
27254 ■	TP-238 (hydrochloride)	CECR2 and BPTF

View all inhibitors of bromodomain-containing proteins at **www.caymanchem.com**

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