
EPIGENETICS &
GENE REGULATION
Cayman
CHEMICAL

# Introduction

Most people grasp genetics as it applies to them as easily as a seahorse grasps things in his surroundings. It begins when a child hears she has her father's eyes and considers how that could be. The father wonders, in turn, if he will get the 'good genes' of his great-grandfather, still alive at 98. In the meantime, Dr. Oz is telling his viewing audience about the links between heart problems and genetics. But where is the discussion, the understanding, the headlines about epigenetics?

Consider this: Gregor Mendel's pea studies were published in the 1860s, when Darwin's *On Origin of the Species* was making the rounds. Conrad Hal Waddington had to understand genetics in order to even suggest an epigenetic landscape, "only" 70 years ago. A query in PubMed using 'epigenetic' as a search term reveals a bounce from 321 publications in 2000 to 1,210 in 2005, jumping again to 4,752 in 2012. A similar search for 'genetics' in PubMed indicates that the same bounce in that field happened in the early 1960s, 50 years ago. Clearly, epigenetics is in its early years.

Cayman Chemical's goal is to help make research possible. In anticipation of a need for better tools for epigenetics research, Cayman has synthesized and purified a collection of research reagents and recombinant proteins to study nucleosomal modification. Furthermore, Cayman has built a dedicated Epigenetic Screening Laboratory and hired scientists to develop assays to profile and screen compounds that modulate epigenetic signaling, described in this catalog. Moreover, the scientists in our Epigenetic Screening Laboratory can provide screening and profiling services according to your needs.

Visit **www.caymanchem.com/episcreen** for more information.

# Abbreviations

| | |
|---|---|
| **ADP** | Adenosine Diphosphate |
| **ChIP** | Chromatin Immunoprecipitation |
| **DNA** | Deoxyribonucleic Acid |
| **$EC_{50}$** | Half maximal effective concentration |
| **ELISA** | Enzyme-linked Immunosorbent Assay |
| **ER** | Estrogen Receptor |
| **Gcn5** | General control of amino acid synthesis protein |
| **GSK** | Glycogen Synthase Kinase |
| **GST** | Glutathione S-Transferase |
| **HAT** | Histone Acetyltransferase |
| **HDAC** | Histone Deacetylase |
| **His** | Histidine |
| **$IC_{50}$** | Half maximal inhibitory concentration |
| **ICC** | Immunocytochemistry |
| **$ID_{50}$** | Infectious dose |
| **IF** | Immunofluorescence |
| **IHC** | Immunohistochemistry |
| **IP** | Immunoprecipitation |
| **JmjC** | Jumonji C |
| **LSD** | Lysine-Specific Demethylase |
| **MLL** | Mixed-Lineage Leukemia or Myeloid/Lymphoid Leukemia |
| **NAD** | Nicotinamide Adenine Dinucleotide |
| **NF-κB** | Nuclear Factor κ-light-chain-enhancer of activated B cells |
| **NSD** | Nuclear Receptor SET domain-containing protein |
| **PAD** | Protein Arginine Deiminase |
| **PHD** | Plant Homeodomain |
| **PRMT** | Protein Arginine Methyltransferase |
| **RNA** | Ribonucleic Acid |
| **SCID** | Severe Combined Immunodeficiency |
| **SIR** | Silent Information Regulator |
| **SIRT** | Sirtuin |
| **WB** | Western Blot |

**Ordering Information**
Orders are accepted by telephone, fax, mail, e-mail, or *via* the Cayman Chemical website. We will accept telephone orders Monday through Friday from 8 AM to 6 PM EST. All orders received by 1 PM EST will be shipped the same day if stock is available (Monday through Thursday only). Confirming purchase orders must be clearly marked as such to avoid possibility of duplication.

**Domestic Shipments**
In most instances we ship FedEx Standard Overnight Delivery (not available to all locations), with delivery by 3:30 PM of the next business day. Product availability may vary. Local delivery is available for the Ann Arbor area only. Other shipping options will be considered upon request, but can be granted only under conditions that will ensure the quality of the product. Freight is prepaid and added to the invoice. Please inquire at the time of order for an estimate of the freight charges. If you wish us to ship collect, please supply a valid account number when ordering. Please address all orders to:

**Cayman Chemical Company**
**1180 E. Ellsworth Road**
**Ann Arbor, MI 48108 USA**
**Phone: (734) 971-3335**
**Toll-free Phone: (800) 364-9897**
**Fax: (734) 971-3640**
**E-mail: custserv@caymanchem.com**
**www.caymanchem.com**

**Include the following information with your order:**
1. Catalog number, description, size, and quantity desired.
2. Complete shipping address. (Delivery is not available to post office box numbers.)
3. A complete billing address.
4. A purchase order number or major credit card (Visa, MasterCard, or American Express), account number, and expiration date.
5. Name of the end user.

**Terms**
1. U.S. funds only, drawn on a U.S. bank.
2. Net 30 days.
3. F.O.B. Ann Arbor, Michigan, U.S.A.
4. Bank fees and wire transfer fees are not to be deducted from the invoice amount.

**Returns**
Products cannot be returned without prior authorization from Cayman Chemical Company. Please contact our Customer Service Department for return shipping instructions. Custom orders and radioactive material cannot be accepted for return credit if due to a customer's error.

**Technical Assistance**
Technical assistance is available from 8 AM to 5:30 PM EST. If inquiring about a purchased product, please provide the catalog number, lot number, and date of purchase to our technical staff so they may answer your questions quickly. Technical assistance may be reached toll free at 888-526-5351, *via* e-mail at techserv@caymanchem.com, or on the web at www.caymanchem.com/techserv.

**Use of Research Products**
The products in this catalog are not for human or veterinary disease diagnosis or therapeutic drug use. They should be used only by technically qualified individuals or those under their direct supervision. Any individual working directly with these products should have free access to the applicable Material Safety Data Sheet (MSDS) and should read and understand it completely prior to use. Please contact our Customer Service Department or visit the specific product page on our website if you require additional copies of any MSDS.

**Patent Disclaimer**
The end-user assumes full responsibility for appropriate licensing and/or non-infringement for any proprietary claim or patent.

**Warranty and Limitation of Remedy**
Cayman Chemical Company makes no warranty or guarantee of any kind, whether written or oral, expressed or implied, including without limitation, any warranty of fitness for a particular purpose, non infringement, suitability, and merchantability, which extends beyond the description of the chemicals hereof. Cayman warrants only to the original customer that the material will meet our specifications at the time of delivery. Cayman will carry out its delivery obligations with due care and skill. Thus, in no event will Cayman have any obligation or liability, whether in tort (including negligence) or in contract, for any direct, indirect, incidental, or consequential damages, even if Cayman is informed about their possible existence. This limitation of liability does not apply in the case of intentional acts or negligence of Cayman, its directors or its employees. Buyer's exclusive remedy and Cayman's sole liability hereunder shall be limited to a refund of the purchase price, or at Cayman's option, the replacement, at no cost to Buyer, of all material that does not meet our specifications. Said refund or replacement is conditioned on Buyer giving written notice to Cayman within thirty (30) days after arrival of the material at its destination. Failure of Buyer to give said notice within thirty (30) days shall constitute a waiver by Buyer of all claims hereunder with respect to said material. Neither party shall be liable to the other in any manner for the failure of or delay in the fulfillment of all or part of their obligations, resulting from causes or circumstances beyond their reasonable control including, but not limited to, floods, fires, hurricanes, tornadoes, earthquakes, other natural calamities and extraordinary weather, insurrections, wars, acts of terrorism, riots, embargoes, governmental refusals to issue approval for export, other governmental orders or restrictions, shortages of shipping vehicles, delays in transportation, inability to obtain supplies and materials, strikes, and lockouts.



# Epigenetics & Gene Regulation

# DNA Methylation

## establishing & editing the methylome

by [Olivia L. May, Ph.D.]

Throughout our lifespan, chemical changes subtly occur in our DNA. A comparison of the DNA of a newborn baby with that of a centenarian shows that the scope of these changes can be dramatic, potentially having an influence on disease.[1] This may help explain why our risk of cancer and other diseases increases as we get older. Such exogenous influences can also be inherited, impacting the genetics of an individual's offspring. Epigenetic regulation involves genetic control by factors other than an individual's DNA sequence. These heritable changes alter DNA accessibility and chromatin structure, thereby regulating patterns of gene expression. Through epigenetic programming, genes are switched on or off as needed to determine which proteins are transcribed and expressed. This process is crucial to normal development (controlling genomic imprinting and X-chromosome inactivation) as well as for the suppression of transposable elements and the maintenance of stable cellular identities. Unfortunately, changes in DNA methylation patterns also contribute to human diseases, like cancer, for which risk increases with age.

DNA methylation, the chemical process that adds a methyl group to DNA, is the principal manner in which genes are transcriptionally repressed or silenced. This modification occurs specifically at CpG sites, regions in which a cytosine nucleotide is located next to a guanine nucleotide that is linked by a phosphate (Figure 1). Inserting methyl groups changes the appearance and structure of DNA, which may directly block DNA recognition and binding of transcription factors, or may attract other factors that preferentially bind to DNA to interfere with transcription factor accessibility. Three families of proteins which bind methylated DNA have been identified so far.[2,3] These include MBD domain proteins, Kaiso and Kaiso-like proteins, and SRA domain proteins. By recruiting these proteins, DNA methylation marks can promote the persistence of certain histone states, such as deacetylation, thus enabling posttranslational histone modifications. As an example, methyl CpG-binding domain protein 2 (MeCP2), a member of the MBD family, binds to methyl CpG and recruits HDACs, which promote chromosome condensation and transcriptional repression.

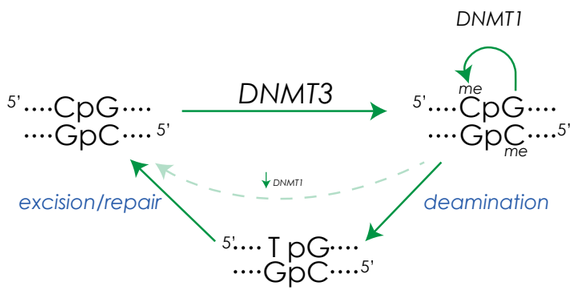



**Figure 1. DNA methylation and demethylation.** *De novo* DNA methylation at the cytosine in CpG dinucleotides is initiated by DNMT3A and DNMT3B. After replication, DNMT1 maintains the methylation state in the daughter strands. Base excision repair mechanisms facilitate removal of methylation after deamination of methyl cytosine (5mC) creates a T:G mismatch.

### Establishing methylation marks

CpG sites are methylated by one of three DNA methyltransferases (DNMTs). During embryogenesis, *de novo* methylation is typically performed by DNMT3A and DNMT3B. Both have similar structures, comprising a PWWP domain, PHD-like or ADD domain, and a carboxy-terminal catalytic domain. The PWWP domains are necessary for binding of DNMT3A and DNMT3B to chromatin *in vivo*. DNMT3L, which lacks the PWWP and a functional catalytic domain, forms a heterotetramer with DNMT3A or DNMT3B and stimulates the activity of its *de novo* partners, guiding the recognition of DNA targets.[4] The PHD domain of DNMT3L interacts with the animo terminal tail of histone H3 and is activated only when bound to unmethylated DNA.[5]

Appropriate combinations of histone modifications create either protective or permissive conditions for the docking of *de novo* methylation complexes. Specific methylation of the lysine at residue 4 (H3K4) by SETD1 inhibits DNMT3L binding. H3K4 methylation is a marker for active genes, and there is an inverse correlation between the presence of trimethylated H3K4 and DNA methylation at promoters.[5,6] Indeed, chromatin at the majority of unmethylated CpGS is enriched in H3K4 di- and tri-methylation. Removal of H3K4 methylation by the histone demethylase LSD2 (KDM1B) is required for establishment of DNA methylation at the promoters of certain imprinted genes. Additionally, DNMT3A binding is promoted by SETD2 trimethylation of lysine 36 of histone 3 (H3K36me3), whereas the H3K36me2 demethylase KDM2A binds to unmethylated CpGs resulting in depletion of H3K36me2.[6] Many questions still remain however as to where and how patterns of methylation are established to target appropriate, region-specific histone modifications.[7]

### Maintaining methylation marks for long term stability

The DNA methylation patterns established during embryonic development are faithfully copied through somatic cell divisions in order to maintain a gene's transcriptionally active or inactive state. The ubiquitously expressed DNMT1 is predominantly responsible for maintaining cellular levels of CpG methylation. With guidance from the UHRF1 domain it recognizes hemimethylated DNA and methylates appropriate cytosines in newly synthesized daughter strands formed during replication (Figure 1). The base pairing of CpG allows for the reciprocal preservation of methylation during subsequent replication cycles. CpG islands keep their overall unmethylated state (or possibly methylated state) extremely stably through multiple cell generations, and DNMT1 is partly responsible for this stability.

In early embryogenesis, following sex-determination of the embryo, methylation is erased throughout the genome (in order to reset germ-cell specification) and then reestablished in all but CpG islands.[8] This guarantees renewal of totipotency at each generation allowing new methylation marks to be established.[9] As developmental differentiation proceeds, these marks accumulate especially in promoter or other gene regulatory regions to repress transcription of certain key pluripotency genes. This cycle of early embryonic demethylation followed by *de novo* methylation is critical in determining somatic DNA methylation patterns. Once established, somatic DNA methylation (a nongenetic trait) is passed through daughter cell generations, and with it, the contextual effects on gene expression. Methylation is considered a long-term, relatively stable epigenetic trait that contributes to maintenance of the cellular phenotype. While a significant fraction of CpG islands are prone to progressive methylation in certain tissues to maintain permanent cell lines, *de novo* methylation also occurs in mature somatic cells, especially in abnormal cells such as cancers.

### Fine-tuning methylation marks

The removal of CpG methylation predictably occurs in cellular reprogramming during gametogenesis, after zygote fertilization, or to preserve induced pluripotency. This demethylation process requires the action of both cytidine deaminases and DNA repair mechanisms (Figure 1). Enzymatic deamination of 5-methylcytosine (5mC) leads to formation of thymine and T:G base-pair mismatches. Base excision repair mechanisms subsequently delete thymine and restore C:G base pairing during epigenetic reprogramming. Spontaneous deamination of 5mC also requires base excision repair mechanisms to repair base-pairing mismatch. This process is highly inefficient in most differentiated cells, however, as spontaneous deamination of 5mC typically results in an overall depletion of CpG dinucleotide sequences. Until very recently, CpG methylation was considered long-lasting and difficult to eliminate post-differentiation, save for inactivation of DNTMs or after spontaneous deamination and mismatch repair. DNA methylation marks were generally thought to be lost 'passively' by lack of DNA methylation maintenance at replication (Figure 1), resulting in progressive loss of methylation at each cell division.[10]

> *"With the recent discovery that cytosines can be hydroxymethylated to 5-hydroxymethylcytosine (5hmC), an active mechanism for demethylation has since been eagerly endorsed."*

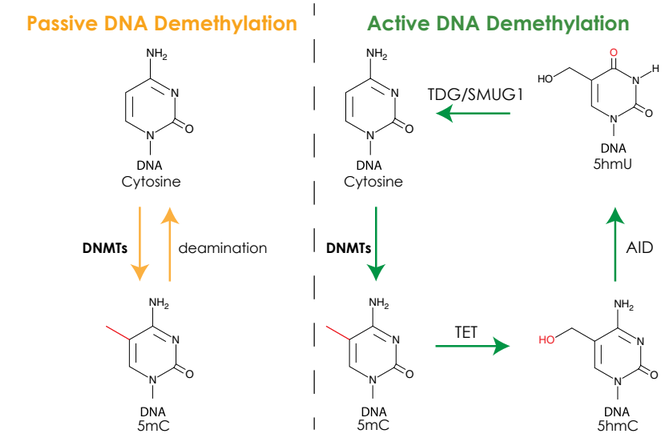



**Figure 2. Potential mechanism of passive and active DNA demethylation.** Passive DNA demethylation was thought to occur by a reduction in activity or absence of DNMTs. Active DNA demethylation involves 3 different enzyme families to enable DNA repair: (1) 5-methylcytosine (5mC) is hydroxylated by TET to form 5-hydroxymethylcytosine (5hmC). (2) 5mC (or 5hmC) is deaminated by AID to form 5-methyluracil (5mU) or 5-hydroxymethyluracil (5hmU). (3) TDG and SMUG1 base excision repair (BER) glycosylases replace these intermediates (5hmU), culminating in cytosine replacement and DNA demethylation.

With the recent discovery that cytosines can be hydroxymethylated to 5-hydroxymethylcytosine (5hmC), an active mechanism for demethylation has since been eagerly endorsed (Figure 2).[11] 5hmC, which impairs remethylation by DNMTs until it is replaced by DNA repair, has been hypothesized to serve as an intermediate in the removal of methylated cytosines. Three different enzyme families are thought to drive active demethylation: the ten-eleven translocation (TET) family, the AID (Activation-Induced cytidine Deaminase) family, and a family of base excision repair (BER) glycosylases (Figure 2). TET has been shown to hydroxylate and then further oxidize methylated cytosines to catalyze their conversion to 5hmC. Targeting specific hydroxymethylated loci, AID deaminates 5hmC to uracil (5hmU), which is eventually replaced with an unmethylated cytosine by thymine-DNA glycosylase (TDG) and single-strand-selective monofunctional uracil-DNA glycosylase 1 (SMUG1).

Thus, DNA methylation is proving to be a dynamic process, requiring continuous regulation and potentially having an important editing role for cellular signaling or tissue-specific differentiation. Further understanding of the nuances of addition and removal of methylation marks on DNA will continue to inspire therapeutic strategies for targeting DNA methylation in the prevention of cancer and other human diseases.[12-14] In contribution to this effort, Cayman offers several potent DNMT inhibitors including the nucleoside analogs: 5-Azacytidine (Item No. 11164), Decitabine (Item No. 11166), and Zebularine (Item No. 10975) as well as the less cytotoxic, non-nucleoside analog: RG-108 (Item No. 13302).

For article references see **page 64**

# Histones & Chromatin Regulators

## Antibodies



## Proteins



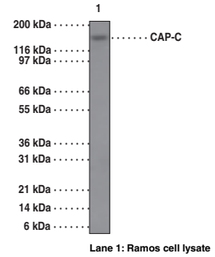
### Chromosome Associated Protein-C Polyclonal Antibody (aa 281-297) 13501

*CAP-C*

Protein G-purified IgG **Stability:** ≥1 year at -20°C

**Summary:** Antigen: human CAP-C amino acids 281-297 • Host: rabbit • Cross Reactivity: (+) human CAP-C • Application(s): WB • CAP-C plays a critical role in the structural maintenance of chromosomes, including proper condensation and segregation.

1 ea




Lane 1: Ramos cell lysate

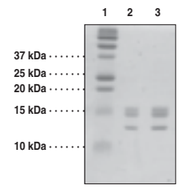
### Core Histones (human) 11010

*HeLa Core Histones*

**Purity:** ≥95% **Stability:** ≥6 months at -80°C

**Source:** Highly purified mixture of human core histones (H2A, H2B, H3, and H4) isolated *via* hydroxyapatite chromatography from HeLa S3 (human cervical adenocarcinoma) nuclear pellet • A histone octamer consists of two copies of each of the core histones, H2A, H2B, H3, and H4 which dimerize to create the nucleosome core.

25 µg
50 µg
100 µg




Lane 1: MW Markers
Lane 2: Core Histones (1 µg)
Lane 3: Core Histones (2 µg)

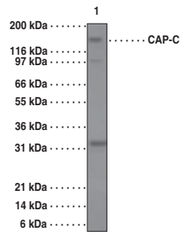
### Chromosome Associated Protein-C Polyclonal Antibody (aa 47-61) 13503

*CAP-C*

Protein G-purified IgG **Stability:** ≥1 year at -20°C

**Summary:** Antigen: human CAP-C amino acids 47-61 • Host: rabbit • Cross Reactivity: (+) human CAP-C • Application(s): WB • CAP-C plays a critical role in the structural maintenance of chromosomes, including proper condensation and segregation.

1 ea



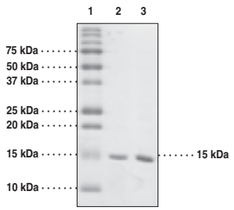

Lane 1: Ramos cell lysate

### Histone H2A (*Xenopus* recombinant) 10261

**$M_r$:** 13.9 kDa **Purity:** ≥95% **Stability:** ≥6 months at -80°C

Lyophilized powder **Source:** Recombinant protein consisting of amino acids 1-129 expressed in *E. coli* • Histone 2A is one of the four histones that comprise a nucleosome protein core.

50 µg
100 µg
250 µg
1 mg




Lane 1: MW Markers
Lane 2: H2A (1 µg)
Lane 3: H2A (2 µg)



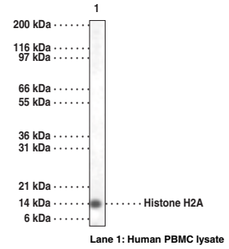


### Histone H2A Polyclonal Antibody 13535

Protein G-purified IgG **Stability:** ≥1 year at -20°C

**Summary:** Antigen: human histone H2A amino acids 1-15 and 81-96 • Host: rabbit • Cross Reactivity: (+) human and mouse histone H2A • Application(s): ELISA and WB • Histone H2A is one of the five main histone proteins involved in the structure of chromatin in eukaryotic cells. It is considered a core histone and forms a dimer with H2B; the core molecule is complete when H3-H4 also attaches to form a tetramer.

1 ea



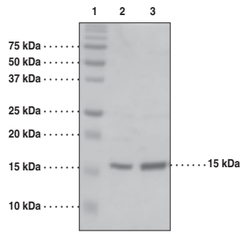

Lane 1: Human PBMC lysate

### Histone H2B (*Xenopus* recombinant) 10262

**$M_r$:** 13.7 kDa **Purity:** ≥95% **Stability:** ≥6 months at -80°C

Lyophilized Powder **Source:** Recombinant protein consisting of amino acids 1-123 expressed in *E. coli* • Histone H2B is one of the core nucleosomal histones. It undergoes many modifications which include acetylation, methylation, and phosphorylation that are important for regulation of gene transcription.

50 µg
100 µg
250 µg
1 mg



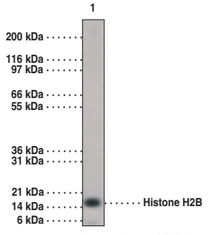

Lane 1: MW Markers
Lane 2: Purified H2B (1 µg)
Lane 3: Purified H2B (2 µg)

### Histone H2B (C-Term) Polyclonal Antibody 13538

Protein G-purified IgG **Stability:** ≥1 year at -20°C

**Summary:** Antigen: human histone H2B amino acids 111-125 • Host: rabbit • Cross Reactivity: (+) chicken, canine, *Drosophila*, human, mouse, rat, most mammals, and zebrafish histone H2B • Application(s): WB • Histone H2B is one of the 5 main histone proteins involved in the structure of chromatin in eukaryotic cells. It features a main globular domain and a long N-terminal tail and forms a dimer with H2A to compose part of the nucleosome core.

1 ea



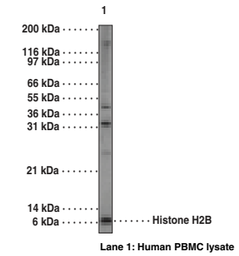

Lane 1: Human PBMC lysate

### Histone H2B (N-Term) Polyclonal Antibody 13539

Protein G-purified IgG **Stability:** ≥1 year at -20°C

**Summary:** Antigen: human histone H2B • Host: rabbit • Cross Reactivity: (+) human histone H2B • Application(s): WB • Histone H2B is one of the 5 main histone proteins involved in the structure of chromatin in eukaryotic cells. It features a main globular domain and a long N-terminal tail and forms a dimer with H2A to compose part of the nucleosome core.

1 ea



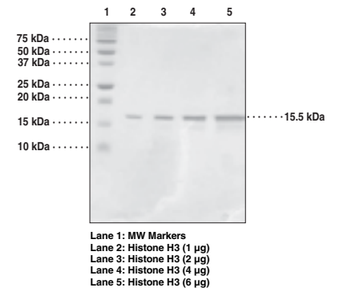

Lane 1: Human PBMC lysate

### Histone H3 (human recombinant) 10263

**$M_r$:** 15.5 kDa **Purity:** ≥95% **Stability:** ≥6 months at -80°C

Lyophilized powder **Source:** Recombinant protein consisting of amino acids 1-136 expressed in *E. coli* • Histone H3 is one of the core nucleosomal histones. It undergoes many modifications which include acetylation, methylation, and phosphorylation that are important for regulation of gene transcription.

50 µg
100 µg
250 µg
1 mg




Lane 1: MW Markers
Lane 2: Histone H3 (1 µg)
Lane 3: Histone H3 (2 µg)
Lane 4: Histone H3 (4 µg)
Lane 5: Histone H3 (6 µg)

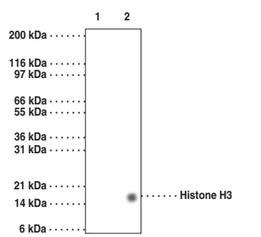
### Histone H3 (Phospho-Ser[28]) Monoclonal Antibody (Clone 117C826) 13540

*PHH3*

Protein G-purified IgG **Stability:** ≥1 year at -20°C

**Summary:** Antigen: human histone H3 • Host: mouse, clone 117C826 • Cross Reactivity: (+) human histone H3 • Application(s): WB • H3 phosphorylation at serine 28 is coupled with mitotic chromosome condensation in diverse mammalian cell lines.

1 ea




Lane 1: Untreated Jurkat cell lysate
Lane 2: FAS-antibody treated Jurkat cell lysate

## Histone H3 Peptide Substrate (1-21) 10877

*H3 Peptide*
**FW:** 2,280.7 **Purity:** ≥95% by HPLC
A lyophilized peptide **Stability:** ≥1 year at -20°C
**Summary:** A target substrate for several of the histone modifying enzymes including lysine methyltransferases, arginine methyltransferases, acetyltransferases, and others.

1 mg

## Histone H3 Trimethyl Lys9 Peptide 10530

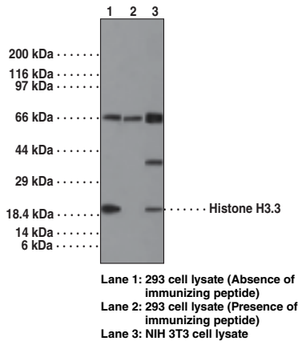
*H3K9me3 Peptide*
**FW:** 1,601 **Peptide Sequence:** ARTKQTARK(Me)$_3$-STGGKA
A lyophilized peptide **Stability:** ≥1 year at -20°C
**Summary:** Peptide contains a trimethylated lysine residue at position nine which is a substrate for several of the JmjC domain-containing class of histone demethylases; JMJD2A and JMJD2D exhibit higher affinity with H3K9me3 compared to H3K9me2

1 mg

## Histone H3.3 Polyclonal Antibody 13784

*H3.3A, H3.3B, H3F3A, H3F3B*
Protein A-purified IgG **Stability:** ≥1 year at -20°C
**Summary:** Antigen: human histone H3.3 amino acids 100-136 • Host: rabbit • Cross Reactivity: (+) chicken, ovine, *Drosophila*, equine, human, mouse, and opossum histone H3.3 • Application(s): IHC and WB • Histone H3.3 constitutes the predominant form of histone H3 in non-dividing cells and is incorporated into chromatin independently of DNA synthesis. It has a central role in transcription regulation, DNA repair, DNA replication, and chromosomal stability.

1 ea

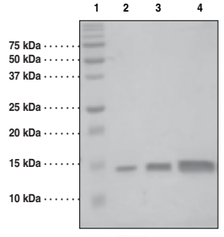



**Lane 1: 293 cell lysate (Absence of immunizing peptide)**
**Lane 2: 293 cell lysate (Presence of immunizing peptide)**
**Lane 3: NIH 3T3 cell lysate**

## Histone H4 (human recombinant) 10264

**$M_r$:** 11.5 kDa **Purity:** ≥95% **Stability:** ≥6 months at -80°C
Lyophilized powder **Source:** Recombinant protein consisting of amino acids 1-103 expressed in *E. coli* • Histone H4 is one of the core nucleosomal histones. The N-terminal tail of histone H4 undergoes many modifications which include acetylation, methylation, and phosphorylation that are important for regulation of gene transcription.

50 µg
100 µg
250 µg
1 mg




**Lane 1: MW Markers**
**Lane 2: Purified H4 (0.5 µg)**
**Lane 3: Purified H4 (1 µg)**
**Lane 4: Purified H4 (2 µg)**

## Histone H4 Peptide Substrate (1-21) 10854

*H4 Peptide*
**FW:** 2,091.5 **Purity:** ≥95% by HPLC
A lyophilized peptide **Stability:** ≥1 year at -20°C
**Summary:** A target substrate for several of the histone modifying enzymes including lysine methyltransferases, arginine methyltransferases, acetyltransferases, and others.

1 mg

## Histone H4 Peptide Substrate (15-24) 10380

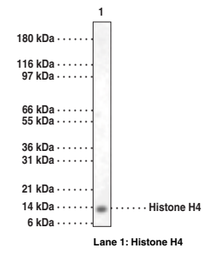
*Histone H4K20 Peptide, SET8 Methyltransferase Acceptor Peptide*
**FW:** 1,278 **Peptide Sequence:** AKRHRKVLRD-NH$_2$
Peptide lyophilized from ammonium bicarbonate buffer **Stability:** ≥1 year at -20°C
**Summary:** Peptide contains a lysine at position 20 which is a substrate or acceptor peptide for the lysine methyltransferases KMT5A (SET8) and KMT5B (SUV4-20H1)

1 mg
5 mg

## Histone H4 Polyclonal Antibody 13543

Protein G-purified IgG **Stability:** ≥1 year at -20°C
**Summary:** Antigen: human histone H4 amino acids 15-30 • Host: rabbit • Cross Reactivity: (+) human histone H4 • Application(s): WB • Histone H4 is a structural component of the nucleosome and is subject to covalent modification including acetylation and methylation, which may alter expression of genes located on DNA associated with its parent histone octamer.

1 ea

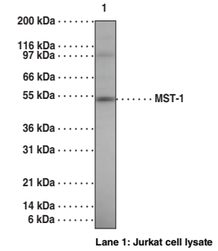



**Lane 1: Histone H4**

## Mammalian STE-20-Like Kinase 1 Polyclonal Antibody 13776

*KRS2, MST-1, STK4*
Protein G-purified IgG **Stability:** ≥1 year at -20°C
**Summary:** Antigen: human MST-1 amino acids 372-390 • Host: rabbit • Cross Reactivity: (+) human MST-1 • Application(s): WB • MST-1 is a serine/threonine kinase that has been implicated in the promotion of chromatin condensation.

1 ea




**Lane 1: Jurkat cell lysate**





# Acetyltransferases

## Antibodies



## Biochemicals



## Kits



## Proteins



## Acetyl Lysine Monoclonal Antibody (Clone 7F8) 10010567

Purified IgG$_1$ lyophilized **Stability:** ≥1 year at -20°C
**Summary:** Antigen: Acetylated KLH • Host: mouse • Isotype: IgG$_1$• Cross Reactivity: (+) acetylated lysine residues; (-) non-acetylated lysine residues • Application(s): ELISA, ICC, and WB • This antibody is useful for monitoring levels of acetylation on various proteins (*e.g.*, histones and p53).

1 ea

## Acetyl Lysine Polyclonal Antibody-biotin 13725

Rabbit immunoglubulin in PBS **Stability:** ≥1 year at -20°C
**Summary:** Antigen: acetylated KLH • Host: rabbit • Cross Reactivity: (+) acetylated lysine residues; (-) non-acetylated proteins • Application(s): ELISA, IF, IP, and WB • This biotin-tagged antibody is useful for monitoring levels of acetylation on various proteins.

400 µl

## Acetyl Lysine Polyclonal Antibody HRP Conjugate 13726

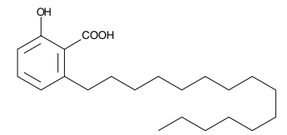
Rabbit immunoglubulin in PBS **Stability:** ≥1 year at -20°C
**Summary:** Antigen: acetylated KLH • Host: rabbit • Cross Reactivity: (+) multi-species • Application(s): ELISA, IF, IP, and WB • This HRP-conjugated antibody is useful for monitoring levels of acetylation on various proteins.

400 µl

## Anacardic Acid 13144

*[16611-84-0] 6-pentadecyl Salicylic Acid*
**MF:** $C_{22}H_{36}O_3$ **FW:** 348.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** An alkyl salicylic acid isolated from cashew shells; inhibits the HAT activity of p300 and pCAF ($IC_{50}$ = 8.5 and 5 µM, respectively); suppresses NF-κB activation, inhibits IκB-α phosphorylation, and prohibits p65 nuclear translocation

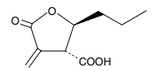
1 mg
5 mg
10 mg
25 mg




## Butyrolactone 3 12095

*[778649-18-6]*
**MF:** $C_9H_{12}O_4$ **FW:** 184.2 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** Specifically inhibits the histone acetyltransferase Gcn5 ($IC_{50}$ = 100 µM) and can inhibit pre-RNA splicing with an $IC_{50}$ value of 0.5 mM

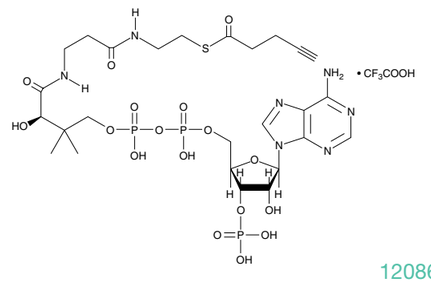
1 mg
5 mg




## 4-pentynoyl-Coenzyme A (trifluoroacetate salt) 10547

*Click Tag™ 4-pentynoyl-CoA*
**MF:** $C_{26}H_{40}N_7O_{17}P_3S \bullet CF_3COOH$ **FW:** 961.6 **Purity:** ≥95%
A lyophilized powder **Stability:** ≥2 years at -20°C
**Summary:** An acyl-CoA donor that can be metabolically transferred onto lysine residues of proteins by lysine acetyltransferases; an azide-alkyne bioconjugation reaction, known as 'click chemistry', can then be used to tag the acetylated proteins with fluorescent or biotinylated labels for subsequent analysis

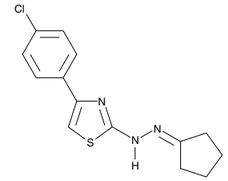
500 µg
1 mg
5 mg
10 mg




## CPTH2 12086

*[357649-93-5]*
**MF:** $C_{14}H_{14}ClN_3S$ **FW:** 291.8 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** Specifically inhibits Gcn5-dependent acetylation of histone H3K14 at a concentration of 0.8 mM both *in vitro* and *in vivo*

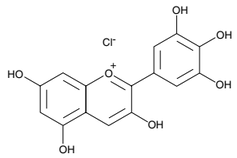
5 mg
10 mg



## Delphinidin chloride 11012

*[528-53-0] Ephdine*
**MF:** $C_{15}H_{11}ClO_7$ **FW:** 338.7 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** A natural plant pigment which induces the release of nitric oxide by vascular endothelium, causing vasorelaxation; inhibits signaling through EGFRs, suppressing the expression of ERα and inducing both apoptosis and autophagy at a dose of 1-40 µM; inhibits the HAT activities of p300/CBP ($IC_{50}$ = ~ 30 µM)

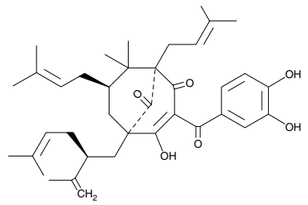
1 mg
5 mg
10 mg




## Garcinol 10566

*[78824-30-3] Camboginol*
**MF:** $C_{38}H_{50}O_6$ **FW:** 502.8 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** An inhibitor of the HATs p300 and pCAF ($IC_{50}$ = 7 and 5 µM, respectively) that also inhibits the HAT Gcn5; promotes neurogenesis and *ex vivo* expansion of human hematopoietic stem cells; induces apoptosis in several types of cancer cells and has anti-inflammatory actions

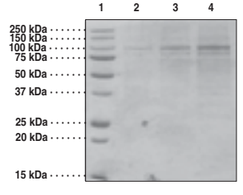
1 mg
5 mg
10 g
25 g




## Gcn5 (human recombinant) 10782

*General control of amino acid synthesis protein 5-like 2, KAT2A, Lysine acetyltransferase 2A, STAF97*
**$M_r$:** 96.3 kDa **Purity:** ≥80% **Stability:** ≥6 months at -80°C
**Source:** Active recombinant N-terminal His-tagged protein consisting of amino acids 2-837 expressed in *Sf*21 cells • Recombinant Gcn5 preferentially acetylates lysine 14 on histone H3 *in vitro*; however, alone it is unable to acetylate nucleosomal core histone substrates. Acetylation of the nucleosomal histones requires that Gcn5 be a part of either the multisubunit SAGA or ATAC protein complexes, which have a broad substrate specificity, including H3K9, H3K18, H4K8, and H4K16, as well as additional sites on histone H2B.

25 µg
50 µg
100 µg




Lane 1: MW Markers
Lane 2: Gcn5 (1 µg)
Lane 3: Gcn5 (2 µg)
Lane 4: Gcn5 (4 µg)

## HAT Inhibitor Screening Assay Kit 10006515

*Histone Acetyltransferase*
**Stability:** ≥1 year at -20°C
**Summary:** Cayman's HAT Inhibitor Screening Assay Kit provides a fast, fluorescence-based method for evaluating pCAF HAT inhibitors. The procedure requires only three easy steps, all performed in the same microwell plate. In the first step of the protocol, HAT is incubated with acetyl-CoA and the histone H3 peptide. During this time, HAT catalyzes the enzymatic transfer of acetyl groups from acetyl-CoA to the H3 peptide producing an acetylated peptide and CoASH. Following addition of isopropanol to stop the enzymatic reaction, CPM is added to the wells of the plate. CPM reacts with the free thiol groups present on CoASH forming a highly fluorescent product that is detected using excitation and emission wavelengths of 360-390 and 450-470 nm, respectively.

96 wells

## pCAF Histone Acetyltransferase 10009115

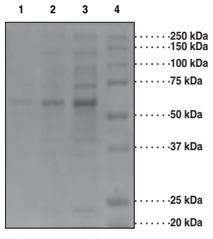
*HAT, p300/(CREB binding protein) Associated Factor*
**$M_r$:** ~40 kDa **Purity:** ≥95% **Stability:** ≥6 months at -80°C
**Source:** Active recombinant GST-tagged protein consisting of amino acids 2-837 expressed in *E. coli* • pCAF belongs to the GCN5/pCAF family of nuclear HATs. Cayman's pCAF preparation contains 165 amino acids from the HAT activity domain of human pCAF fused to GST at the N-terminus. Enzyme activity was determined using a fluorescent HAT assay and is comparable to that found in the literature.

25 µg
50 µg
100 µg

## TIP60 (human recombinant) 10783

*cPLA(2) Interacting Protein, Esa1, HIV-1 Tat Interacting Protein 60 kDa, Hs.6364, HTATIP, KAT5, PLIP*
**$M_r$:** 60.3 kDa **Purity:** ≥80% **Stability:** ≥6 months at -80°C
**Source:** Active recombinant N-terminal His-tagged protein consisting of amino acids 2-513 expressed in *Sf*21 cells • TIP60 is a member of the MYST family of lysine acetyl transferases. It has been shown to acetylate histones, p53, and the Ataxia Telangiectasia Mutant protein kinase.

25 µg
50 µg
100 µg




Lane 1: TIP60 (5 µg)
Lane 2: TIP60 (10 µg)
Lane 3: TIP60 (20 µg)
Lane 4: MW Markers

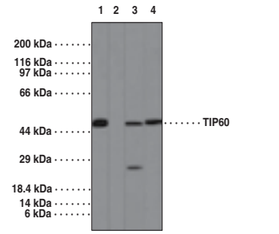




## TIP60 Polyclonal Antibody 13789

*KAT5, Lysine Acetyltransferase 5*
Protein A-purified IgG **Stability:** ≥1 year at -20°C
**Summary:** Antigen: peptide within the region of human TIP60 amino acids 480-530 • Host: rabbit • Cross Reactivity: (+) human (isoform CRA_b), chimpanzee, orangutan, equine, canine, mouse, ovine, rat, opossum, zebrafish, and *Xenopus* TIP60 • Application(s): IHC and WB • TIP60 belongs to the MYST family of HATs. It is a catalytic subunit of the NuA4 HAT complex which is involved in transcriptional activation of select genes principally by acetylation of nucleosomal histones H4 and H2A.

1 ea




Lane 1: Human brain lysate (Absence of immunizing peptide)
Lane 2: Human brain lysate (Presence of immunizing peptide)
Lane 3: Mouse brain lysate
Lane 4: Rat brain lysate

# Deacetylases

## Antibodies

| | | |
|---|---|---|
| 15 | 13493 | HDAC3 Polyclonal Antibody |
| 15 | 13494 | HDAC4 Polyclonal Antibody |
| 15 | 13499 | HDAC6 Polyclonal Antibody |
| 15 | 13500 | HDAC7 (Phospho-Ser$^{155}$) Polyclonal Antibody |
| 18 | 13504 | HDAC11 Polyclonal Antibody |
| 18 | 13778 | Metastasis Associated 1 Family Member 2 Polyclonal Antibody |
| 19 | 13785 | p66α Polyclonal Antibody |
| 22 | 13477 | SIRT7 Polyclonal Antibody |

## Biochemicals

| | | |
|---|---|---|
| 12 | 13145 | AGK2 |
| 12 | 14004 | AK-7 |
| 12 | 10575 | Apicidin |
| 13 | 89740 | CAY10398 |
| 13 | 10005019 | CAY10433 |
| 13 | 10009797 | CAY10591 |
| 13 | 13146 | CAY10603 |
| 13 | 13172 | CBHA |
| 13 | 13686 | Chidamide |
| 13 | 12084 | CI-994 |
| 13 | 10009798 | EX-527 |
| 13 | 10576 | HC Toxin |
| 13 | 13277 | (S)-HDAC-42 |
| 18 | 13295 | HNHA |
| 18 | 10641 | JGB1741 |
| 18 | 13174 | M 344 |
| 18 | 13284 | MS-275 |
| 19 | 13176 | Oxamflatin |
| 19 | 10444 | PCI 34051 |
| 19 | 13212 | Pimelic Diphenylamide 106 |
| 19 | 13870 | Pyroxamide |
| 19 | 10009929 | SAHA |
| 19 | 10675 | SAHA-BPyne |
| 19 | 10671 | coumarin-SAHA |
| 20 | 10495 | 4-iodo-SAHA |
| 20 | 13178 | Salermide |
| 20 | 10443 | SB 939 |
| 20 | 10572 | Scriptaid |
| 23 | 10523 | Sirtinol |
| 23 | 13121 | Sodium Butyrate |
| 23 | 13168 | Splitomicin |
| 23 | 10574 | Suberohydroxamic Acid |
| 23 | 13085 | Tenovin-1 |
| 23 | 13086 | Tenovin-6 |
| 23 | 89730 | Trichostatin A |
| 23 | 10559 | Tubastatin A (trifluoroacetate salt) |
| 23 | 13033 | Valproic Acid (sodium salt) |

## Kits

| | | |
|---|---|---|
| 14 | 10011563 | HDAC Activity Assay Kit |
| 14 | 600150 | HDAC Cell-Based Activity Assay Kit |
| 14 | 10011564 | HDAC1 Inhibitor Screening Assay Kit |
| 18 | 700230 | HDAC8 Inhibitor Screening Assay Kit |
| 20 | 10010401 | SIRT1 Direct Fluorescent Screening Assay Kit |
| 21 | 10010991 | SIRT1 FRET-Based Screening Assay Kit |
| 20 | 700280 | SIRT2 Direct Fluorescent Screening Assay Kit |
| 21 | 10011566 | SIRT3 Direct Fluorescent Screening Assay Kit |
| 21 | 700290 | SIRT6 Direct Fluorescent Screening Assay Kit |

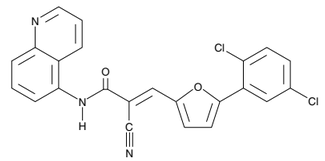
## Proteins

| | | |
|---|---|---|
| 14 | 10009231 | HDAC1 (human recombinant) |
| 14 | 10009377 | HDAC2 (human recombinant) |
| 14 | 10009232 | HDAC3/NCOR2 (human recombinant) |
| 15 | 10009652 | HDAC4 (human recombinant) |
| 15 | 10009379 | HDAC5 (human recombinant) |
| 15 | 10009465 | HDAC6 (human recombinant) |
| 15 | 19380 | HDAC8 (human recombinant) |
| 18 | 10009466 | HDAC9 (human recombinant) |
| 19 | 11633 | NCOR2/SMRT (human recombinant) |
| 21 | 10011190 | SIRT1 (human recombinant) |
| 21 | 10011191 | SIRT2 (human recombinant) |
| 22 | 10011194 | SIRT3 (human recombinant) |
| 22 | 10317 | SIRT4 (human recombinant) |
| 22 | 10318 | SIRT5 (human recombinant) |
| 22 | 10315 | SIRT6 (human recombinant) |
| 22 | 10316 | SIRT7 (human recombinant) |

### AGK2 — 13145

*[304896-28-4]*
**MF:** $C_{23}H_{13}Cl_2N_3O_2$ **FW:** 434.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** A cell-permeable, selective inhibitor of SIRT2 ($IC_{50}$ = 3.5 µM) that minimally affects either SIRT1 or SIRT3; rescues dopamine neurons from α-synuclein toxicity in both *in vitro* and *in vivo* Parkinson's disease models

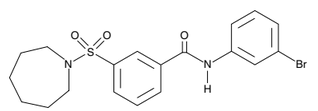
1 mg
5 mg
10 mg
25 mg



### AK-7 — 14004

*[420831-40-9]*
**MF:** $C_{19}H_{21}BrN_2O_3S$ **FW:** 437.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** A cell- and brain-permeable inhibitor of SIRT2 ($IC_{50}$ = 15.5 µM); dimishes neuronal cell death induced by mutant huntingtin fragment in culture; down-regulates cholesterol biosynthetic gene expression and reduces total cholesterol levels in neurons *in vivo*

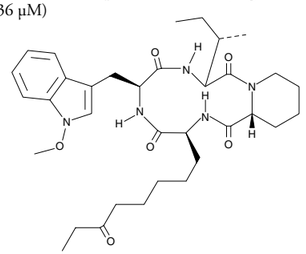
5 mg
25 mg



### Apicidin — 10575

*[183506-66-3] OSI 2040*
**MF:** $C_{34}H_{49}N_5O_6$ **FW:** 623.8 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** A fungal toxin that demonstrates selective inhibition of HDAC3/NcoR over HDAC6 ($IC_{50}$s = 15.8 and 665.1 nM, respectively); has broad spectrum activity against Apicomplexan parasites and exhibits antiproliferative activity against various cancer cell lines ($IC_{50}$s = 0.13-2.36 µM)

1 mg
5 mg
10 mg



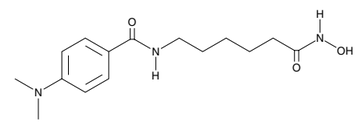




### CAY10398 — 89740

*[193551-00-7] MD 85, PX 089274*
**MF:** $C_{15}H_{23}N_3O_3$ **FW:** 293.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** An inhibitor of HDAC ($IC_{50}$ = 10 µM)

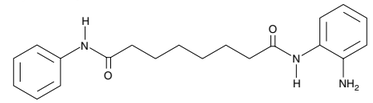
1 mg
5 mg
10 mg
25 mg



### CAY10433 — 10005019

*[537034-17-6] BML-210, N-phenyl-N'-(2-Aminophenyl)hexamethylenediamide*
**MF:** $C_{20}H_{25}N_3O_2$ **FW:** 339.4 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** An HDAC inhibitor with an $IC_{50}$ value of 30 µM when tested in HeLa cell nuclear extracts using 200 µM acetylated fluorometric substrate

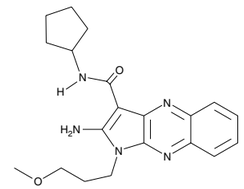
1 mg
5 mg
10 mg
25 mg



### CAY10591 — 10009797

*[839699-72-8] SIRT1 Activator 3, Sirtuin 1 Activator 3*
**MF:** $C_{20}H_{25}N_5O_2$ **FW:** 367.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** An activator of SIRT1 that decreases TNF-α levels from 325 pg/ml (control) to 104 and 53 pg/ml at 20 and 60 µM, respectively; exhibits a significant dose-dependent effect on fat mobilization in differentiated adipocytes

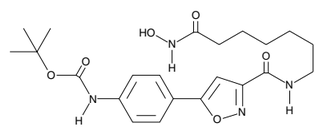
1 mg
5 mg
10 mg
25 mg



### CAY10603 — 13146

*[1045792-66-2]*
**MF:** $C_{22}H_{30}N_4O_6$ **FW:** 446.5 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** A potent and selective inhibitor of HDAC6 ($IC_{50}$ = 0.002 nM, as compared with 271, 252, 0.42, 6851, and 90.7 nM for HDAC1, 2, 3, 8, and 10, respectively); prevents the growth of several pancreatic cancer cell lines ($IC_{50}$ = 0.1-1 µM)

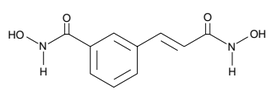
500 µg
1 mg
5 mg
10 mg



### CBHA — 13172

*[174664-65-4] m-Carboxycinnamic Acid bis-Hydroxamine, HDAC Inhibitor II*
**MF:** $C_{10}H_{10}N_2O_4$ **FW:** 222.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** HDAC1 and HDAC3 inhibitor ($ID_{50}$ = 0.01 and 0.07 µM, respectively, *in vitro*); induces apoptosis in nine different neuroblastoma cell lines in culture (0.5-4.0 µM) and completely suppresses neuroblastoma tumor growth in SCID mice at 200 mg/kg

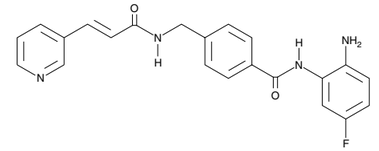
5 mg
10 mg
25 mg
50 mg



### Chidamide — 13686

*[743420-02-2]*
**MF:** $C_{22}H_{19}FN_4O_2$ **FW:** 390.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** An HDAC inhibitor that increases histone H3 acetylation levels in LoVo and HT29 colon cancer cells at concentrations as low as 4 µM; dose-dependently decreases the activation of several oncogenic signaling kinases and induces cell cycle arrest in colon cancer cells

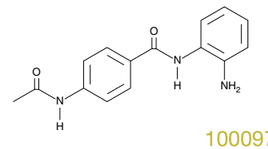
1 mg
5 mg
10 mg
25 mg



### CI-994 — 12084

*[112522-64-2] N-Acetyldinaline, Goe 5549, PD 123654, Tacedinaline*
**MF:** $C_{15}H_{15}N_3O_2$ **FW:** 269.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** An inhibitor of class I HDACs with $IC_{50}$ values of 0.9, 0.9, 1.2, and >20 µM for recombinant human HDAC 1, 2, 3, and 8, respectively; displays a wide spectrum of antitumor activity, particularly in tumors normally refractory to conventional anticancer agents

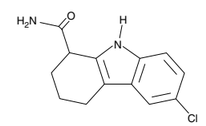
5 mg
10 mg
50 mg



### EX-527 — 10009798

*[49843-98-3]*
**MF:** $C_{13}H_{13}ClN_2O$ **FW:** 248.7 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** A cell-permeable, selective inhibitor of SIRT1 ($IC_{50}$ = 98 nM); inhibits other SIRTs only at much higher concentrations and has no effect on other HDACs

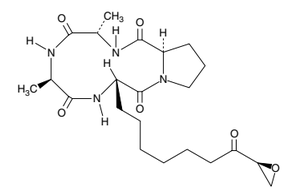
1 mg
5 mg
10 mg
25 mg



### HC Toxin — 10576

*[83209-65-8] Toxin I (Helminthosporium carbonum)*
**MF:** $C_{22}H_{34}N_4O_6$ **FW:** 450.5 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** A cell-permeable, reversible inhibitor of HDACs ($IC_{50}$ = 30 nM)

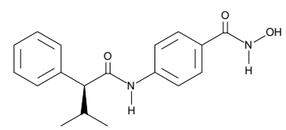
500 µg
1 mg



### (S)-HDAC-42 — 13277

*[935881-37-1] AR42*
**MF:** $C_{18}H_{20}N_2O_3$ **FW:** 312.4 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** A potent inhibitor of HDACs ($IC_{50}$ = 16 nM *in vitro*); decreases the viability of prostate cancer cell lines ($IC_{50}$ = 0.40 µM); strongly suppresses the growth of PC-3 tumor xenografts

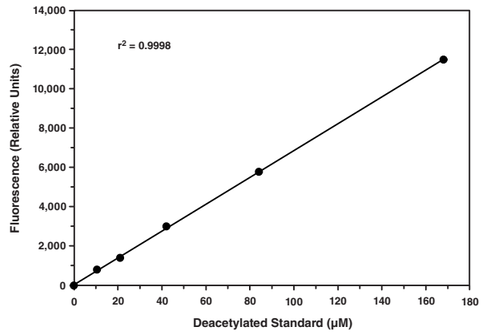
1 mg
5 mg
10 mg
25 mg



## HDAC Activity Assay Kit 10011563

**Stability:** ≥1 year at -80°C
**Summary:** Cayman's HDAC Activity Assay Kit provides a fast, fluorescence-based method for measuring Class I and II HDAC activity that eliminates radioactivity, extraction, or chromatography. The procedure requires only two easy steps, both performed in the same microplate. The fluorescent reaction product is analyzed using a plate reader with excitation wavelengths of 340-360 nm and emission wavelengths of 440-465 nm.

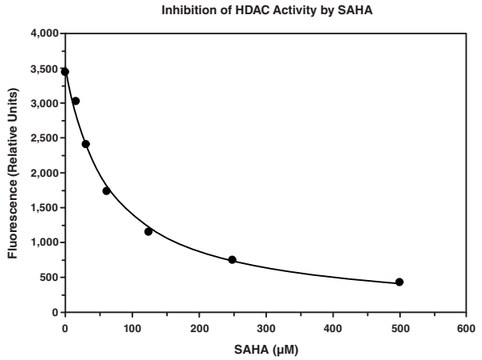
96 wells




## HDAC Cell-Based Activity Assay Kit 600150

**Stability:** ≥6 months at -80°C
**Summary:** Cayman's HDAC Cell-Based Assay Kit provides an easy tool for studying HDAC activity modulators in whole cells. By using a cell-permeable HDAC substrate, the activity of various protein lysine-specific deacetylases including HDAC1-containing complexes can be measured in intact cells in a simple and homogenous manner. The fluorescence of the deacetylated reaction product can be analyzed using a plate reader or a fluorometer with excitation wavelengths of 340-360 nm and emission wavelengths of 440-465 nm. An HDAC inhibitor, trichostatin A, is included for checking specificity of the HDAC reaction. This assay parallels Cayman's HDAC Activity Assay Kit (Item No. 10011563), which uses a nuclear extract rather than whole cells for the assay. Together, both assays will help to identify whether an inhibitor/activator has a direct effect on the enzyme.

96 wells




## HDAC1 (human recombinant) 10009231

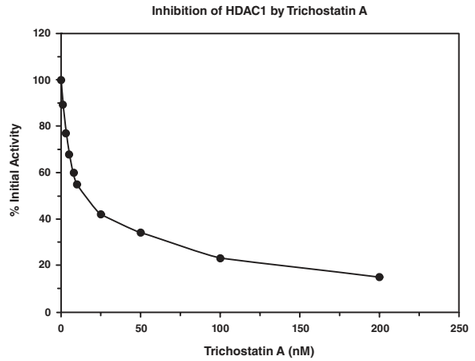
**$M_r$:** ~79.9 kDa **Purity:** >10% by SDS-PAGE **Stability:** ≥6 months at -80°C
**Source:** Active recombinant protein containing a C-terminal GST-tag expressed in *Sf*21 cells • HDAC1 is a Class I HDAC that catalyzes the deacetylation of core histones and other non-histone proteins to control complex biological events, including cell development, differentiation, programmed cell death, angiogenesis, and inflammation.

1 ea

## HDAC1 Inhibitor Screening Assay Kit 10011564

**Stability:** ≥1 year at -80°C
**Summary:** Cayman's HDAC1 Inhibitor Screening Assay Kit provides a fast, fluorescence-based method for screening HDAC1 inhibitors. The procedure requires only two easy steps, both performed in the same microplate. The fluorescent reaction product is analyzed using a fluorometer with excitation wavelengths of 340-360 nm and emission wavelengths of 440-465 nm. Sufficient purified HDAC1 is provided for 96 assays.

96 wells




## HDAC2 (human recombinant) 10009377

**$M_r$:** ~60 kDa **Purity:** ≥70% by SDS-PAGE **Stability:** ≥6 months at -80°C
**Source:** Active full-length recombinant protein containing a C-terminal His-tag expressed in *Sf*9 cells • HDAC2 is a Class I HDAC that catalyzes the deacetylation of core histones, resulting in tightening of nucleosomal integrity, restricting access to transcription factors, and suppression of transcription.

1 ea

## HDAC3/NCOR2 (human recombinant) 10009232

**$M_r$:** ~49.7 kDa **Purity:** ≥50% **Stability:** ≥6 months at -80°C
**Source:** Active recombinant protein containing a complex of human HDAC3 with a C-terminal His-tag and human NCOR2 amino acids 395-489 with an N-terminal GST-tag • HDAC3 is a Class I HDAC that is inactive alone and requires binding with the deacetylase activation domain of NcoR2 for activation.

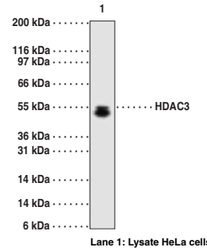
1 ea



## HDAC3 Polyclonal Antibody 13493

Protein G-purified IgG **Stability:** ≥1 year at -20°C
**Summary:** Antigen: human HDAC3 amino acids 2-17 • Host: rabbit • Cross Reactivity:(+) human HDAC3 • Application(s): ChIP, IP, and WB • HDAC3 is a class I HDAC that plays an important role in cell development, differentiation, programmed cell death, angiogenesis, and inflammation.

1 ea




## HDAC4 (human recombinant) 10009652

**$M_r$:** 75.2 kDa **Purity:** ≥50% **Stability:** ≥6 months at -80°C
**Source:** Active N-terminal GST-tagged protein consisting of amino acids 627-1,085 expressed using a baculovirus expression system • HDAC4 is a Class IIa HDAC that can shuttle between the nucleus and cytoplasm, suggesting potential extranuclear functions by regulating the acetylation status of nonhistone substrates.

1 ea

## HDAC4 Polyclonal Antibody 13494

Protein G-purified IgG **Stability:** ≥1 year at -20°C
**Summary:** Antigen: human HDAC4 amino acids 194-209 • Host: rabbit • Cross Reactivity: (+) human and mouse HDAC4 • Application(s): ChIP, IP, and WB • HDAC4 is a class II HDAC that can shuttle between the nucleus and cytoplasm, suggesting potential extranuclear functions by regulating the acetylation status of non-histone substrates.

1 ea




## HDAC5 (human recombinant) 10009379

**$M_r$:** 51 kDa **Purity:** ≥90% **Stability:** ≥6 months at -80°C
**Source:** Active recombinant protein consisting of amino acids 657-1,123 with a C-terminal His-tag expressed in *Sf*9 cells • HDAC5 is a Class IIa HDAC that can shuttle between the nucleus and cytoplasm, suggesting potential extranuclear functions by regulating the acetylation status of non-histone substrates.

1 ea

## HDAC6 (human recombinant) 10009465

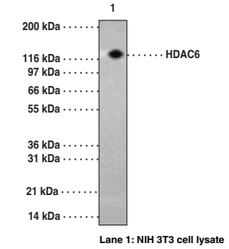
**$M_r$:** ~159 kDa **Purity:** ≥80% **Stability:** ≥6 months at -80°C
**Source:** Active recombinant protein with an N-terminal GST-tag expressed in *Sf*9 cells • HDAC6 is a Class II HDAC that can shuttle between the nucleus and cytoplasm, suggesting potential extranuclear functions by regulating the acetylation status of non-histone substrates.

1 ea

## HDAC6 Polyclonal Antibody 13499

Protein G-purified IgG **Stability:** ≥1 year at -20°C
**Summary:** Antigen: human HDAC6 amino acids 1-16 • Host: rabbit • Cross Reactivity: (+) human and mouse HDAC6 • Application(s): ChIP, IP, and WB • HDAC6 is a class II HDAC that can shuttle between the nucleus and cytoplasm, suggesting potential extranuclear functions by regulating the acetylation status of non-histone substrates.

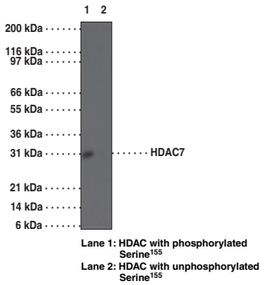
1 ea




## HDAC7 (Phospho-Ser$^{155}$) Polyclonal Antibody 13500

Protein G-purified IgG **Stability:** ≥1 year at -20°C
**Summary:** Antigen: peptide from human HDAC7 containing phospho-Ser$^{155}$ • Host: rabbit • Cross Reactivity: (+) chimpanzee, bovine, canine, human, monkey, mouse, and rat HDAC7 • Application(s): WB • HDAC7 is a class IIa HDAC that plays a specific role in maintaining vascular integrity by repressing the expression of matrix metalloproteinase 10. It promotes repression mediated by transcriptional corepressor NCOR2 and is an efficient corepressor of the androgen receptor. It is also responsible for the deacetylation of lysine residues on the N-terminal part of the core histones.

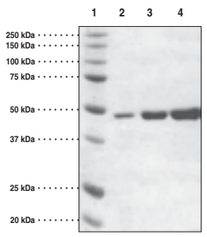
1 ea




## HDAC8 (human recombinant) 19380

**$M_r$:** 45.3 kDa **Purity:** ≥95% **Stability:** ≥6 months at -80°C
**Source:** Active recombinant protein containing a C-terminal His-tag expressed in *E. coli* • HDAC8 is a Class I HDAC that catalyzes the deacetylation of core histones, resulting in tightening of nucleosomal integrity, restricting access to transcription factors, and suppression of transcription. It can also play an important role in mediating nuclear receptor functions by forming co-repressor complexes with nuclear receptors in the absence of ligands.

25 µg
50 µg
100 µg



# HISTONE

## Acetylation, Deacetylation, & Genomic Bistability

by [Thomas G. Brock, Ph.D.]

If you search PubMed using the keyword 'epigenetics', you'll find over 5,500 papers. Closer inspection will reveal that almost half were published in the last two years! This rapid growth of the field reflects, at least in part, a broadening definition of the term. The original concept of epigenetics, developed in the late 20th century, focused on changes at the nuclear level that are heritable but do not involve changes in the DNA sequence. In that vision, such changes should be passed on for at least one generation, whether that is a mitotic division (at the cellular level) or an offspring (in complex organisms). In the new millennium, epigenetics has come to embrace an ever-increasing number of nuclear events which alter gene expression without changing DNA sequence. The absolute requirement for heritability has been lessened, replaced by an interest in histone and nucleosomal modification.

The study of histone acetylation and deacetylation has benefitted from these changes. The acetylation of histones has been described for decades, and early studies showed that acetylation status changed during cell division or development. Interest grew markedly when histone deacetylases were found to alter chromatin structure and regulate gene transcription. However, concerns that acetylation marks are not maintained as cells divide has brought into question whether these enzymes are truly involved in epigenetic processes.[1] This concern considers de/acetylation by itself, whereas models embracing the complexity of histone modification suggest roles for acetyl marks in heritable expression states. This article touches on these issues.

### Histone Acetylases and Deacetylases

Acetylation refers to the addition of an acetyl group ($CH_3CO$) to organic compounds. Histone acetyltransferases (HATs) catalyze the transfer of an acetyl group from acetyl-CoA to the terminal amine on the side chain of lysine residues; since many HATs also acetylate lysine (denoted 'K') on other proteins, there is also a KAT nomenclature for most HATs (Table 1). While the twenty or so human HATs have a common general enzymatic capacity, they actually diverge in function, with some pairs of HATs showing overlap in histone targets. Importantly, most HATs contain distinct binding domains in addition to the acetyltransferase domain. For example, the MYST enzymes contain a C2HC-type zinc finger domain for binding other molecules, while CBP and P300 have bromodomains for binding acetylated lysine residues. This means that each HAT shows certain specificity in both where they bind and where they acetylate. The conversion of the positively charged lysine to non-charged acetyl-lysine, like the addition of negative phosphates to uncharged amino acids during phosphorylation, alters protein structure and interactions with other biomolecules. For example, acetylation of histones typically promotes the recruitment of effector proteins, relaxation of chromatin conformation, and an increase in transcription.

Like phosphorylation, acetylation is reversible. Histone deacetylases (HDACs, aka KDACs) are a smaller group of evolutionarily conserved enzymes. The human class I HDACs are homologous to the yeast enzyme Rpd3 and include HDAC1, 2, 3, and 8. Class II HDACs are homologous to yeast Hda1 and are divided into class IIa (HDAC4, 5, 7, 9) and class IIb (HDAC6 and 10) based on structure. The human class III HDACs, homologous to the yeast Sir2 protein, include the sirtuin family of $NAD^+$-dependent protein deacetylases (SIRT1-3, 5, 6). The novel HDAC11 has a distinct structure and is a class IV HDAC. The HDACs often participate in the formation of transcriptional repressor complexes, inducing chromatin compaction through histone deacetylation, and silencing gene expression.

| Coding Gene | KAT Name | Site of Histone Modification |
|---|---|---|
| HAT 1 | KAT1 | H2AK5, H4K5, H4K12 |
| GCN5 | KAT2A | H3K9, H3K14, H3K56, H4K5, H4K8, H4K12, H4K16, H4K91 |
| PCAF | KAT2B | H3K9, H3K14 |
| CBP | KAT3A | H3K14, H3K18, H3K27, H3K56, H4K5, H4K8, H4K12, H4K16 |
| P300 | KAT3B | H3K14, H3K18, H3K27, H3K56, H4K5, H4K8, H4K12, H4K16 |
| TAF1 | KAT4 | H3K14 |
| TIP60 | KAT5 | H2AK5, H4K5, H4K8, H4K12, H4K16 |
| MYST3 | KAT6A | H3K9, H3K14 |
| MYST4 | KAT6B | |
| MYST2 | KAT7 | H3K14, H4K5, H4K8, H4K12 |
| MYST1 | KAT8 | H4K16 |
| ELP3 | KAT9 | H3K9, H3K18 |
| GTF3C4 | KAT12 | H3K14 |
| NCOA1 | KAT13A | H3K14 |
| NCOA3 | KAT13B | H3K14 |
| CLOCK | KAT13D | H3K14 |
| CDY1 | | |
| CDY2 | | |
| CDYL | | |
| MGEA5 | | H4K8, H3K14 |
| NAT10 | | |

**Table 1. Some human lysine acetyltransferases**

### The Devil in the Details

Given an assortment of HATs and HDACs, what can we say about how they really work? Let's start with a look at the histones. Nucleosomes consist of DNA wrapped twice around an octamer composed of two sets of the core histones H2A, H2B, H3, and H4, with N-terminal tails of each histone projecting from the structure, as displayed in Figure 1. HATs acetylate lysine residues, which, intriguingly, are regularly spaced along the tails, commonly with 2 or 3 intervening residues. The spacing is apparent whether you look at the primary sequence given in letters or at the secondary structure of the nucleosome (lysines denoted in red). Why might they be spaced in this way? Moreover, most (if not all) lysine residues may be methylated or acetylated, but not both. Thus, most lysines have at least three alternative states: unmarked, acetylated, or methylated. Up to three methyl groups can accumulate on each lysine residue, with one methyltransferase (KMT) usually adding the first group and a second KMT executing the further additions. This suggests that the monomethylated lysine state is distinct from the polymethylated state, since the former is more readily transitioned back to the unmarked residue. If a given lysine state is viewed as a factor in affecting, say, protein binding, then the multiple states of the numerous lysines represents an abundance of information. This is evident without considering the impact of lysine ubiquitination or sumoylation, arginine methylation or citrullination, or phosphorylation of serines and threonines.

Unlike some enzymes, HATs and HDACs rarely work alone. For example, the HAT nuclear receptor coactivator 1 (NCOA1) directly binds dimerized nuclear receptors in a hormone-dependent fashion and, in this context, recruits additional HATs, including P300 and CBP.[2] HDAC1 and HDAC2 bind several partners to form the nucleosome remodeling and histone deacetylation (NuRD) complex that directs both histone deacetylation and ATP-dependent chromatin remodeling. Complexes containing HATs or HDACs bind to DNA or proteins, including modified histones. For example, the HAT-containing NuA3 complex binds methylated histone H3, localizing its HAT closer to the target site, H3K14.[3] Importantly, and perhaps counterintuitively, HAT or HDAC complexes that bind to one nucleosome are not targeting residues on the same nucleosome. Instead, these complexes, typically much bigger than the histone octamers which surround them, may act on multiple histone tails. This is not a trivial point, as it may link acetylation with heritability.

### Genomic Bistability

An iconic image from the earliest days of epigenetics is that of the 'epigenetic landscape', presented by Conrad Hal Waddington in 1932 to visualize the external manifestation of genetic activity in an era when genes were considered discrete heritable units but their structures and functions were yet undiscovered (Figure 2). In this model, meant to pertain to cell differentiation, marbles (cells) move varying ways down a landscape whose contour is affected by genes. Details within the contours are further defined by factors above ('epi-') the fixed genetic level, and these details determine the final resting state of differentiation for each cell type.

Histone modifications may turn over rapidly, suggesting such marks might be too labile to carry information across cell divisions.[4] How might acetylation contribute to heritable changes? This question relates to another topic: bistable systems. Some biological processes are analog and graded, where the output is a varying function of the input and the output returns to baseline when the input is removed. Other processes may be digital, yes-or-no by nature. For example, cell division, fertilization, and apoptosis are directional, digital decisions, as changes between states are hard to reverse. Some biochemical reactions are reversibly bistable, moving between active and inactive states. A simple model of bistability, taken from physics, is reminiscent of Waddington's landscape: particles may have three critical states, two of which represent minimum free energies and the third a maximum free energy (Figure 2). Mathematically, the unstable maximum must lie between the two stable minima and thus represents a barrier.

*"Histone modifications may turn over rapidly, suggesting such marks might be too labile to carry information across cell divisions."*

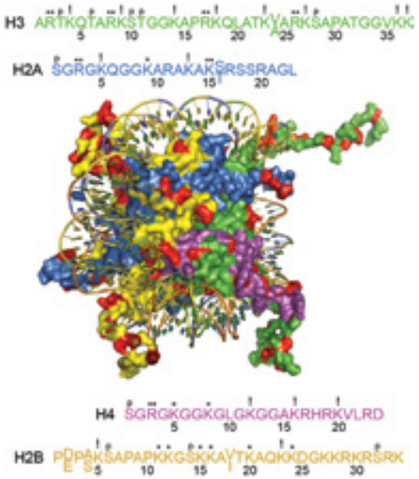



**Figure 1.** Histone tails can have many marks. The amino termini project from the octamer core. N-terminal sequences for each of the core histones are given, with known sites of acetylation (*), methylation (**), either acetylation or methylation (!), or phosphorylation (p) indicated. Lysine residues within the nucleosome are colored in red.

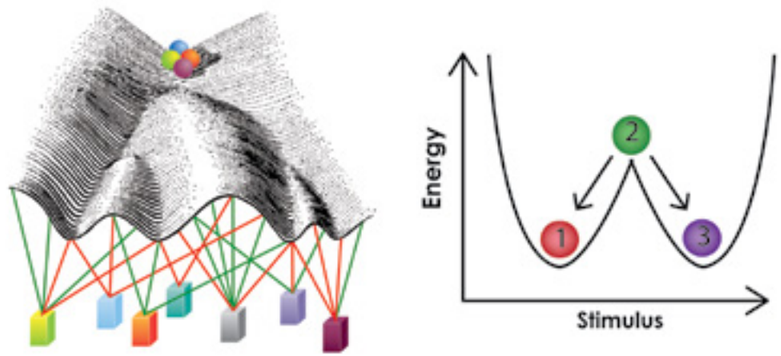



**Figure 2.** Epigenetic valleys (left) are like bistable conditions (right). In epigenetics, differentiation is like contours, affected by underlying genes and 'epi-'genetic factors, shaping cell fate. In bistable systems, two stable states (balls 1 and 3) may be attained from an unstable state (ball 2), depending on the stimulus.

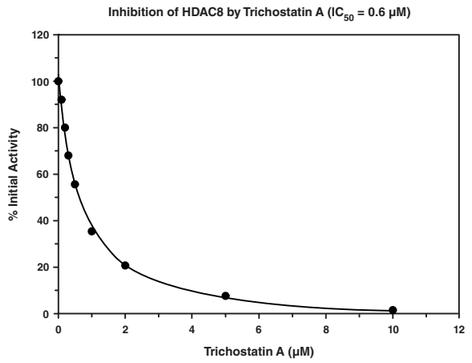
In an early application of bistability theory to epigenetic cell memory, Ian B. Dodd and colleagues start with the understanding that stability depends on positive feedback, where modified nucleosomes recruit enzymes that similarly modify nearby nucleosomes.[5] There are several established examples of histone modifying enzymes that can both recognize and create the same modification.[6-9] For example, CBP both binds acetylated proteins using a bromodomain and acetylates histones and other proteins. Robust stability requires cooperativity of modified nucleosomes in the modification reaction as well as modification beyond nearest neighbors.[5] Current theoretical and empirical research is helping to refine our understanding of bistability in biological processes, including epigenetic signaling. For example, some systems employ multiple positive feedback loops, or combinations of positive and negative feedback loops, as well as spatial or temporal staggering of loops, in order to generate or enhance bistability.[10-12] The assortment of histone marks, in concert with complexes which can read, write, and erase these marks, clearly represents machinery capable of using bistability to provide heritability. The challenge will be to gain insight into how the signals work, how they go awry, and how they might be mended.

For article references see page 64

## HDAC8 Inhibitor Screening Assay Kit 700230

**Stability:** ≥1 year at -80°C
**Summary:** Human HDAC8 is a class I HDAC and has been identified in a variety of human cancer tissues. Cayman's HDAC8 Inhibitor Screening Assay provides a convenient fluorescence-based method for screening HDAC8 inhibitors. The procedure requires only two easy steps, both performed in the same microplate. The fluorescent reaction product is analyzed with an excitation wavelength between 350-360 nm and an emission wavelength between 450-465 nm. Sufficient HDAC8 is provided for 96 assays.

96 wells




## HDAC9 (human recombinant) 10009466

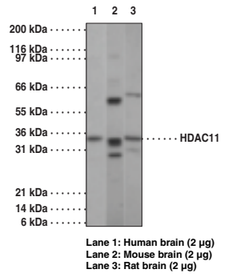
**$M_r$:** ~50.7 kDa **Purity:** ≥95% **Stability:** ≥6 months at -80°C
**Source:** Active recombinant protein consisting of amino acids 604-1,066 wih a C-terminal His-tag expressed in *Sf*9 cells • HDAC9 is a Class IIa HDAC that can shuttle between the nucleus and cytoplasm, suggesting possible extranuclear functions including regulating the acetylation status of non-histone substrates.

1 ea

## HDAC11 Polyclonal Antibody 13504

Protein G-purified IgG **Stability:** ≥1 year at -20°C
**Summary:** Antigen: peptide from human HDAC11 amino acids 182-199 • Host: rabbit • Cross Reactivity: (+) human, mouse, and rat HDAC11 • Application(s): WB • HDAC11 is a class IV HDAC that is expressed in kidney, heart, brain, skeletal muscle, and testis.

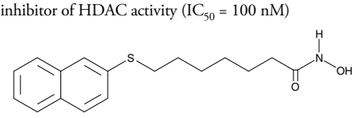
1 ea




## HNHA 13295

*[926908-04-5] Histone Deacetylase Inhibitor VI*
**MF:** $C_{17}H_{21}NO_2S$ **FW:** 303.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** A cell-permeable inhibitor of HDAC activity ($IC_{50}$ = 100 nM)

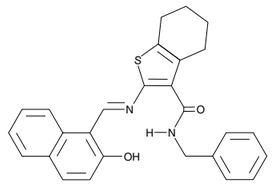
5 mg
10 mg
25 mg
50 mg



## JGB1741 10641

*[1256375-38-8] ILS-JGB-1741*
**MF:** $C_{27}H_{24}N_2O_2S$ **FW:** 440.6 **Purity:** ≥98%
A crystalline solid **Stability:** ≥1 year at -20°C
**Summary:** A SIRT1-specific inhibitor ($IC_{50}$ = 15 µM); inhibits metastatic breast cancer MDA-MB 231 cell proliferation ($IC_{50}$ = 512 nM), dose-dependently increasing p53 acetylation and p53-mediated apoptosis in these cells

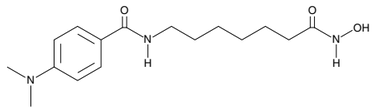
1 mg
5 mg
10 mg
25 mg



## M 344 13174

*[251456-60-7] D237, Histone Deacetylase Inhibitor III, MS 344*
**MF:** $C_{16}H_{25}N_3O_3$ **FW:** 307.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** An inhibitor of HDACs, inhibiting maize HDAC ($IC_{50}$ = 100 nM) as well as human HDAC1 ($IC_{50}$ = 46 nM); shows a 3-fold selectivity for HDAC6 over HDAC1

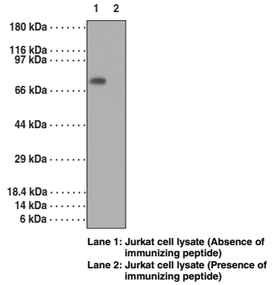
5 mg
10 mg
25 mg
50 mg



## Metastasis Associated 1 Family Member 2 Polyclonal Antibody 13778

*MTA-L1 Protein, MTA2, p53 Target Protein in Deacetylase Complex, PID*
Affinity-purified IgG **Stability:** ≥1 year at -20°C
**Summary:** Antigen: peptide from a portion of human MTA2 amino acids 650-700 • Host: rabbit • Cross Reactivity: (+) chimpanzee, human, and Rhesus monkey MTA2 • Application(s): IHC and WB • MTA2 is a nuclear protein that interacts with HDAC1 and HDAC2 and has a functional role in chromatin remodeling and deacetylase activity. It interacts with p53 and represses p53-dependent transcriptional activation, thereby regulating p53-mediated cell growth arrest and apoptosis.

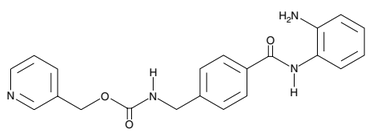
1 ea




## MS-275 13284

*[209783-80-2] Entinostat, SNDX 275*
**MF:** $C_{21}H_{20}N_4O_3$ **FW:** 376.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** An inhibitor of HDACs that preferentially inhibits HDAC1 ($IC_{50}$ = 300 nM) over HDAC3 ($IC_{50}$ = 8 µM); does not inhibit HDAC8; induces p21/C1P1/WAF1, slowing cell growth, differentiation, and tumor development *in vivo*

1 mg
5 mg
10 mg
25 mg







## NCOR2/SMRT (human recombinant) 11633

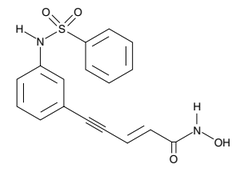
*CTG Repeat Protein 26 , Nuclear Receptor Corepressor 2, Silencing Mediator of Retinoic Acid and Thyroid Hormone Receptor, SMAP270, SMRT, T3 Receptor-Associating Factor, Thyroid-Retinoic-Acid-Receptor-Associated Corepressor, TRAC*
**$M_r$:** 39 kDa **Purity:** ≥60% **Stability:** ≥6 months at -80°C
**Source:** Recombinant N-terminal GST-tagged protein consisting of amino acids 395-489 expressed in *E. coli* • NcoR2 is a transcriptional corepressor that plays an essential role in the regulation of development and metabolism. HDACs can mediate nuclear receptor functions by forming co-repressor complexes with nuclear receptors in the absence of ligands.

50 µg

## Oxamflatin 13176

*[151720-43-3] Metacept 3*
**MF:** $C_{17}H_{14}N_2O_4S$ **FW:** 342.4 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** A potent inhibitor of HDACs ($IC_{50}$ = 15.7 nM); has been shown to alter the expression of several genes whose products are involved in cell morphology, motility, apoptosis, and cell cycle control, reducing the proliferation of cancer cells

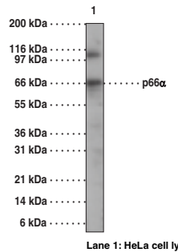
1 mg
5 mg
10 mg



## p66α Polyclonal Antibody 13785

*GATA Zinc Finger Domain-Containing Protein 2A, Transcriptional Repressor p66α*
IgG **Stability:** ≥1 year at -20°C
**Summary:** Antigen: mouse p66α amino acids 572-585 • Host: rabbit • Cross Reactivity: (+) human, mouse, and rat p66α • Application(s): WB • p66 is one of the components of the MeCP1 complex, an HDAC core complex involved in methylated DNA silencing.

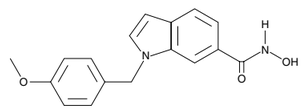
1 ea




## PCI 34051 10444

*[950762-95-5]*
**MF:** $C_{17}H_{16}N_2O_3$ **FW:** 296.3 **Purity:** ≥95%
A crystalline solid **Stability:** ≥1 year at -20°C
**Summary:** A potent HDAC8 inhibitor ($IC_{50}$ = 0.01 µM) with >200-fold selectivity over HDAC isoforms 1, 2, 3, 6, and 10 ($IC_{50}$s = 4, >50, >50, 2.9, and 13 µM, respectively); induces caspase-dependent apoptosis in cell lines derived from T-cell lymphomas or leukemias ($GI_{50}$s = 2.4 - 4 µM)

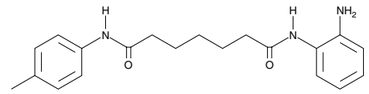
5 mg
10 mg
50 mg
100 mg



## Pimelic Diphenylamide 106 13212

*[937039-45-7] TC-H 106, Histone Deacetylase Inhibitor VII*
**MF:** $C_{20}H_{25}N_3O_2$ **FW:** 339.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥1 year at -20°C
**Summary:** A slow, tight-binding inhibitor of class I HDACs, progressively binding HDACs and remaining bound after wash-out; inhibits class I HDACs ($IC_{50}$ = 150, 760, 370, and 5,000 nM for HDAC1, 2, 3, and 8, respectively) but not class II HDACs ($IC_{50}$ >180 µM for HDAC4, 5, and 7)

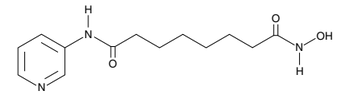
1 mg
5 mg
10 mg
25 mg



## Pyroxamide 13870

*[382180-17-8]*
**MF:** $C_{13}H_{19}N_3O_3$ **FW:** 265.3 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** An inhibitor of HDACs, including HDAC1 ($IC_{50}$ = 0.1-0.2 µM); induces growth suppression and cell death of certain types of cancer cells in culture

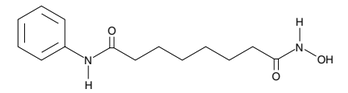
5 mg
10 mg
25 mg
50 mg



## SAHA 10009929

*[149647-78-9] Suberoylanilide Hydroxamic Acid, Vorinostat, Zolinza™*
**MF:** $C_{14}H_{20}N_2O_3$ **FW:** 264.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** An HDAC inhibitor of class I and class II HDACs at around 50 nM; arrests cell growth in a wide variety of transformed cells in culture at 2.5-5.0 µM

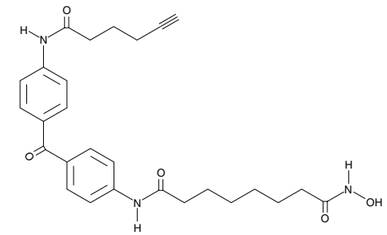
100 mg
250 mg
500 mg
1 g



## SAHA-BPyne 10675

*[930772-88-6] Suberoylanilide Hydroxamic Acid-BPyne*
**MF:** $C_{27}H_{31}N_3O_5$ **FW:** 477.6 **Purity:** ≥98%
A solution in methanol **Stability:** ≥1 year at -20°C
**Summary:** A SAHA derivative with a benzophenone crosslinker and an alkyne tag to be used for profiling HDAC activities in proteomes and live cells; labels HDAC complex proteins both in proteomes at 100 nM and in live cells at 500 nM; $IC_{50}$ = ~3 µM for inhibition of HDAC activity in HeLa cell nuclear lysates in an HDAC activity assay

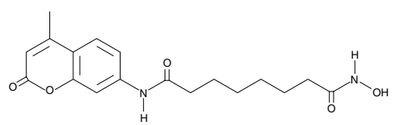
50 µg
100 µg
500 µg



## coumarin-SAHA 10671

*[1260635-77-5] coumarin-Suberoylanilide Hydroxamic Acid*
**MF:** $C_{18}H_{22}N_2O_5$ **FW:** 346.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** A fluorescent probe that competitively binds HDAC; demonstrates fluorescence excitation and emission maxima of 325 and 400 nm, respectively, which is quenched by 50% when bound to HDAC

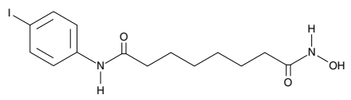
1 mg
5 mg
10 mg
25 mg



## 4-iodo-SAHA 10495

*[1219807-87-0] 4-iodo-Suberoylanilide Hydroxamine Acid*
**MF:** $C_{14}H_{19}IN_2O_3$ **FW:** 390.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** A hydrophobic derivative of the class I and class II HDAC inhibitor SAHA that demonstrates >60% inhibition of HDAC1 and HDAC6 activity in a deacetylase activity assay; inhibits proliferation of SKBR3 breast-derived, HT29 colon-derived, and U937 leukemia cell lines with $EC_{50}$ values of 1.1, 0.95, and 0.12 µM, respectively

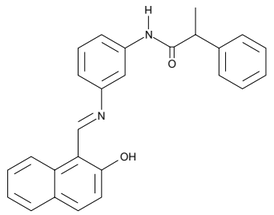
50 mg
100 mg
250 mg
500 mg



## Salermide 13178

*[1105698-15-4]*
**MF:** $C_{26}H_{22}N_2O_2$ **FW:** 394.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** An inhibitor of SIRT1 and SIRT2, causing tumor-specific apoptotic cell death; causes 90% apoptosis within 72 hours ($IC_{50}$~20 µM) by reactivating proapototic genes that are repressed by SIRT1 in MOLT4 leukemia cells

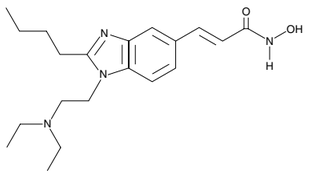
5 mg
10 mg
50 mg
100 mg



## SB 939 10443

*[929016-96-6] Pracinostat*
**MF:** $C_{20}H_{30}N_4O_2$ **FW:** 358.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** A pan-HDAC inhibitor ($IC_{50}$ = 77 nM in an *in vitro* HDAC1 activity assay) that prevents proliferation of ovarian (A2780), colon (COLO 205 and HCT-116), and prostate cancer (PC-3) cell lines at $IC_{50}$ values of 0.48, 0.56, 0.48, and 0.34 µM, respectively; binds all HDAC isozymes with similar affinity ($K_i$s = 16-28 nM) with the exception of HDAC6 and 7 ($K_i$s = 247 and 104 nM, respectively)

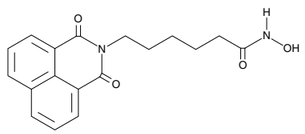
1 mg
5 mg
10 mg
25 mg



## Scriptaid 10572

*[287383-59-9] GCK 1026*
**MF:** $C_{18}H_{18}N_2O_4$ **FW:** 326.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** An HDAC inhibitor that has an optimal effective concentration of 6-8 µM in a cell-based assay, is less toxic than trichostatin A, and works in a wide variety of biological systems; induces cell cycle arrest in cancer cells *in vitro* and *in vivo*; facilitates the cloning of inbred mouse strains produced by somatic cell nuclear transfer

1 mg
5 mg
10 mg
25 mg



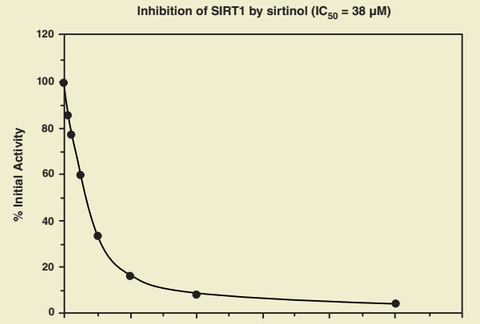
## SIRT Direct Fluorescent Screening Assay Kits

The sirtuins represent a distinct class of trichostatin A-insensitive lysyl-deacetylases (class III HDACs) that catalyze a reaction coupling lysine deacetylation to the formation of nicotinamide and O-acetyl-ADP-ribose. Cayman's Direct Fluorescent Screening Assay Kits provide a convenient fluorescence-based method for screening SIRT inhibitors or activators. The procedure requires only two easy steps, both performed in the same microplate. In the first step, the substrate is incubated with human recombinant SIRT along with its cosubstrate NAD$^+$. Deacetylation sensitizes the substrate such that treatment with the developer in the second step releases a fluorescent product. The fluorophore can be analyzed with an excitation wavelength of 350-360 nm and an emission wavelength of 450-465 nm.

## SIRT1 Direct Fluorescent Screening Assay Kit 10010401

**Stability:** ≥1 year at -80°C

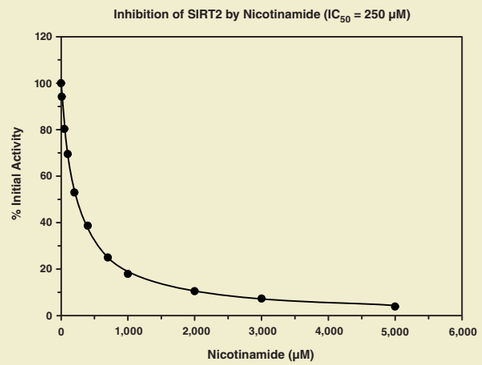
96 wells




## SIRT2 Direct Fluorescent Screening Assay Kit 700280

**Stability:** ≥1 year at -80°C

96 wells



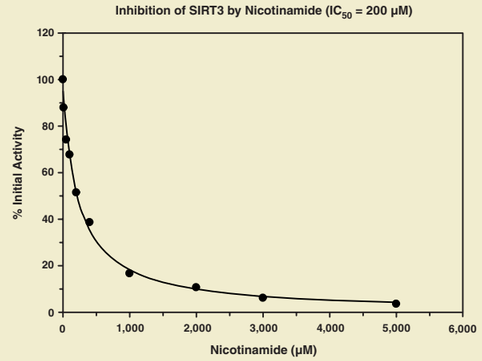





## SIRT3 Direct Fluorescent Screening Assay Kit 10011566

**Stability:** ≥1 year at -80°C

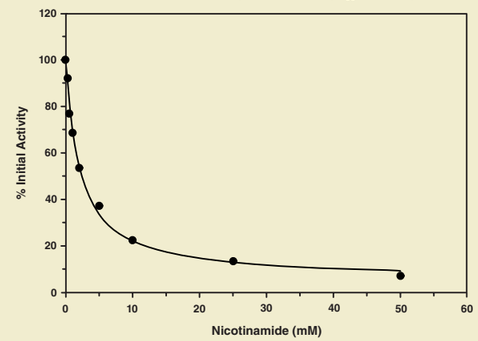
96 wells




## SIRT6 Direct Fluorescent Screening Assay Kit 700290

**Stability:** ≥1 year at -80°C

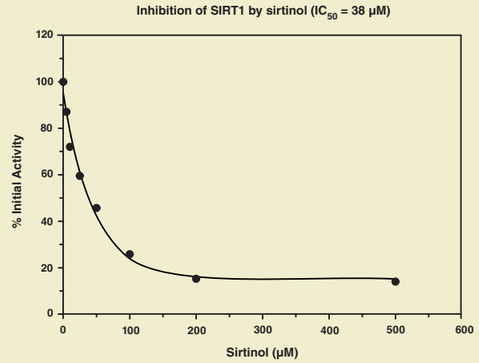
96 wells




## SIRT1 FRET-Based Screening Assay Kit 10010991

**Stability:** ≥1 year at -80°C
**Summary:** Human SIRT1 is the homolog of yeast Sir2 and has been shown to regulate the activity of the p53 tumor suppressor and inhibit apoptosis. Small molecule activators of SIRT1, such as resveratrol, extend lifespan in yeast and *C. elegans* in a manner that resembles caloric restriction. Cayman's SIRT1 FRET-based Screening Assay provides a convenient fluorescence-based method for screening SIRT1 inhibitors or activators. The procedure requires only two easy steps, both performed in the same microplate. In the first step, the substrate, which is coupled to the fluorophore and quencher, is incubated with human recombinant SIRT1 along with its cosubstrate NAD$^+$. Deacetylation sensitizes the substrate such that treatment with the developer in the second step results in the separation of the quencher and fluorophore. The resulting fluorescence is analyzed using an excitation wavelength of 335-345 nm and emission wavelength of 440-465 nm.

96 wells




## SIRT1 (human recombinant) 10011190

*NAD-dependent Deacetylase 1, Silent Information Regulator 2, SIR2L1, SIR2-like Protein 1, Sirtuin 1*
**$M_r$:** 89.2 kDa **Purity:** ≥60% **Stability:** ≥9 months at -80°C
**Source:** Active recombinant N-terminal GST-tagged enzyme amino acids 193-747 expressed in *E. coli* • SIRT1 is the human sirtuin with the greatest homology to yeast Sir2 and has been shown to regulate the activity of the p53 tumor suppressor and inhibit apoptosis.

25 units
50 units
100 units

## SIRT2 (human recombinant) 10011191

*NAD-dependent Deacetylase 2, Silent Information Regulator 2, SIR2L2, SIR2-like Protein 2, Sirtuin 2*
**$M_r$:** 44.2 kDa **Purity:** ≥90% **Stability:** ≥9 months at -80°C
**Source:** Active recombinant N-terminal His-tagged enzyme amino acids 2-389 expressed in *E. coli* • SIRT2 is a cytoplasmic protein responsible for the deacetylation of histone H4 and α-tubulin, a modification important for controlling the cell cycle. SIRT2 co-localizes with HDAC6 and microtubules and functions as a mitotic checkpoint in preventing chromosomal instability that can lead to hyperploid cells.

25 µg
50 µg
100 µg

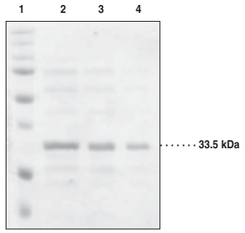
## SIRT3 (human recombinant) 10011194

*Mitochondrial Nicotinamide Adenine Dinuclear-dependent Deacetylase, NAD-dependent Deacetylase 3, Silent Information Regulator 3, SIR2L3, SIR2-like Protein 3, Sirtuin 3*

**$M_r$:** 37 kDa **Purity:** ≥90% **Stability:** ≥9 months at -80°C

**Source:** Active recombinant N-terminal His-tagged enzyme amino acids 101-399 expressed in *E. coli* • SIRT3, is a mitochondrial protein that is synthesized as an enzymatically inactive protein. Human SIRT3 is activated by a matrix-processing peptidase. The constitutive expression of SIRT3 promotes the expression of PGC-1α, UCP1, and other genes involved in mitochondrial functions, indicating that SIRT3 modulates adaptive thermogenesis in BAT.

25 µg
50 µg
100 µg




Lane 1: MW Markers
Lane 2: SIRT3 (5 µg)
Lane 3: SIRT3 (2.5 µg)
Lane 4: SIRT3 (1.25 µg)

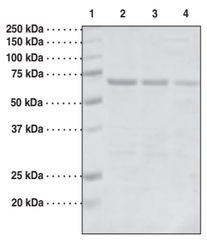
## SIRT4 (human recombinant) 10317

*NAD-dependent ADP-ribosyltransferase Sirtuin 4, Silent Information Regulator 4, SIR2L4, SIR2-like Protein 4, Sirtuin 4*

**$M_r$:** 61.9 kDa **Purity:** ≥95% **Stability:** ≥9 months at -80°C

**Source:** Recombinant N-terminal GST-tagged enzyme expressed in *E. coli* • SIRT4 is a mitochondrial ADP-ribosyltransferase responsible for the transfer of ADP-ribose from NAD to specific substrates such as glutamate dehydrogenase.

25 µg
50 µg
100 µg




Lane 1: MW Markers
Lane 2: SIRT4 (4 µg)
Lane 3: SIRT4 (2 µg)
Lane 4: SIRT4 (1 µg)

## SIRT5 (human recombinant) 10318

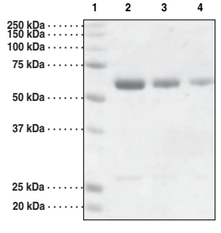
*NAD-dependent Deacetylase 5, Silent Information Regulator 5, SIR2L5, SIR2-like Protein 5, Sirtuin 5*

**$M_r$:** 60.6 kDa (GST-tag); 26 kDa (native) **Purity:** ≥90%

**Stability:** ≥9 months at -80°C

**Source:** Recombinant N-terminal GST-tagged enzyme expressed in *E. coli* • SIRT5 is located in the mitochondrial matrix and its functions are largely still being elucidated, however a few promising substrates have been studied. SIRT5 has been shown to deacetylate carbamoyl phosphate synthetase 1, activating the enzyme to catalyze the first step of the urea cycle.

25 µg
50 µg
100 µg




Lane 1: MW Markers
Lane 2: SIRT5 (4 µg)
Lane 3: SIRT5 (2 µg)
Lane 4: SIRT5 (1 µg)

## SIRT6 (human recombinant) 10315

*NAD-dependent Deacetylase 6, Silent Information Regulator 6, SIR2L6, SIR2-like Protein 6, Sirtuin 6*

**$M_r$:** 43.7 kDa **Purity:** ≥95% **Stability:** ≥6 months at -80°C

**Source:** Active recombinant N-terminal His-tagged enzyme amino acids 1-355 expressed in *E. coli* • SIRT6 associates specifically with telomeres and functions at chromatin to decrease NF-κB signaling. Mammalian cells depleted of SIRT6 display abnormal telomere structures similar to defects found in Werner syndrome, a premature aging disorder associated with a shortened life span.

25 µg
50 µg
100 µg


Lane 1: MW Markers
Lane 2: SIRT6 (2 µg)
Lane 3: SIRT6 (1 µg)
Lane 4: SIRT6 (0.5 µg)

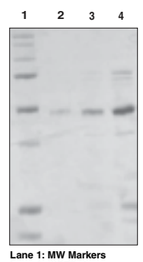
## SIRT7 (human recombinant) 10316

*NAD-dependent deacetylase 7, Silent Information Regulator 7, SIR2L7, SIR2-like protein 7, Sirtuin 7*

**$M_r$:** 49.3 kDa **Purity:** ≥85% **Stability:** ≥6 months at -80°C

**Source:** Recombinant N-terminal His-tagged enzyme amino acids 2-400 expressed in *E. coli* • SIRT7 activates transcription by RNA polymerase I and deacetylates p53. It prevents progressive deterioration of the heart, and is suggested to play an important role in regulation of stress responses and cell death in the heart.

25 µg
50 µg
100 µg




Lane 1: MW Markers
Lane 2: SIRT7 (1 µg)
Lane 3: SIRT7 (2 µg)
Lane 4: SIRT7 (5 µg)

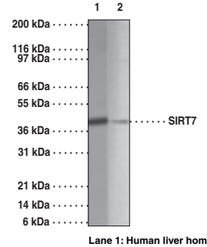
## SIRT7 Polyclonal Antibody 13477

*SIR2, Sirtuin 7*

Protein G-purified IgG **Stability:** ≥1 year at -20°C

**Summary:** Antigen: human SIRT7 amino acids 35-51 and 361-377 • Host: rabbit • Cross Reactivity: (+) human SIRT7 • Application(s): WB • SIRT7 is a member of the sirtuin family of proteins, which are able to metabolize $NAD^+$. Reports of histone-activated SIR2-mediated $NAD^+$ metabolism and $NAD^+$-activated SIR2-mediated histone deacetylation suggest a coupled reciprocal activation mechanism involving interactions of SIR2 with $NAD^+$ and the N-ε-acetyl-lysine groups of acetylated histone.

1 ea




Lane 1: Human liver homogenate
Lane 2: PBMC lysate





## Sirtinol 10523

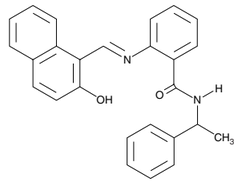
*[410536-97-9] Sir Two Inhibitor Naphthol*

**MF:** $C_{26}H_{22}N_2O_2$ **FW:** 394.5 **Purity:** ≥98%

A crystalline solid **Stability:** ≥2 years at -20°C

**Summary:** A cell-permeable inhibitor of sirtuin $NAD^+$-dependent deacetylases, inhibiting the yeast sirtuin Sir2p with an $IC_{50}$ value of 68 µM and the human sirtuins SIRT1 and SIRT2 with $IC_{50}$ values of 131 and 38 µM, respectively; does not alter HDAC1 activity

1 mg
5 mg
25 mg




## Sodium Butyrate 13121

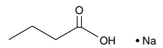
*[156-54-7] Butyric Acid*

**MF:** $C_4H_8O_2$ • Na **FW:** 111.1 **Purity:** ≥95%

A crystalline solid **Stability:** ≥2 years at room temperature

**Summary:** A short chain fatty acid that inhibits HDACs, induces growth arrest, differentiation and apoptosis in cancer cells, and suppresses inflammation by reducing the expression of pro-inflammatory cytokines

50 g
100 g
250 g
500 g




## Splitomicin 13168

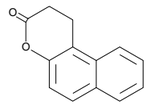
*[5690-03-9] 1-Naphthalenepropanoic Acid*

**MF:** $C_{13}H_{10}O_2$ **FW:** 198.2 **Purity:** ≥98%

A crystalline solid **Stability:** ≥2 years at -20°C

**Summary:** A small molecule inhibitor of Sir2p HDAC activity, displaying higher activity *in vivo* (minimal inhibitory concentration = 0.49 µM) than *in vitro* ($IC_{50}$ = 60 µM); has diverse effects on mammalian cells

5 mg
10 mg
25 mg
50 mg




## Suberohydroxamic Acid 10574

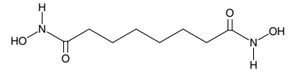
*[38937-66-5] SBHA, Suberic bis-Hydroxamic Acid*

**MF:** $C_8H_{16}N_2O_4$ **FW:** 204.2 **Purity:** ≥98%

A crystalline solid **Stability:** ≥2 years at -20°C

**Summary:** A competitive HDAC inhibitor that inhibits HDAC1 ($IC_{50}$ = 0.25 µM) and HDAC3 ($IC_{50}$ = 0.30 µM); causes cell differentiation, cell cycle arrest, or apoptosis

100 mg
250 mg
500 mg
1 g




## Tenovin-1 13085

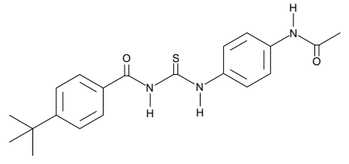
*[380315-80-0]*

**MF:** $C_{20}H_{23}N_3O_2S$ **FW:** 369.5 **Purity:** ≥98%

A crystalline solid **Stability:** ≥2 years at -20°C

**Summary:** A small molecule activator of p53 that decreases the growth of BL2 Burkitt's lymphoma and ARN8 melanoma cells; inhibits the deacetylase activity of purified human SIRT1 and 2

5 mg
10 mg
50 mg
100 mg




## Tenovin-6 13086

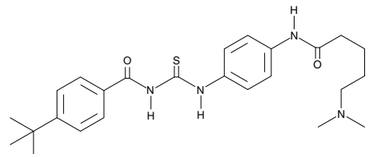
*[1011557-82-6]*

**MF:** $C_{25}H_{34}N_4O_2S$ **FW:** 454.6 **Purity:** ≥95%

A crystalline solid **Stability:** ≥2 years at -20°C

**Summary:** An analog of tenovin-1; elevates p53 activity in MCF-7 cells at 10 µM and reduces growth of ARN8 melanoma xenograft tumors in SCID mice at a dose of 50 mg/kg

1 mg
5 mg
10 mg
25 mg




## Trichostatin A 89730

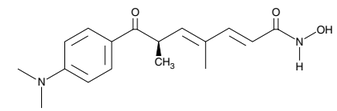
*[58880-19-6] TSA*

**MF:** $C_{17}H_{22}N_2O_3$ **FW:** 302.4 **Purity:** ≥98%

A crystalline solid **Stability:** ≥1 year at -20°C

**Summary:** A potent, reversible inhibitor of HDAC ($IC_{50}$ = 70 nM)

500 µg
1 mg
5 mg
10 mg



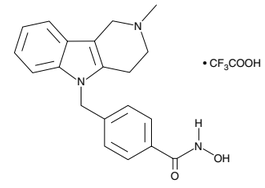

## Tubastatin A (trifluoroacetate salt) 10559

**MF:** $C_{20}H_{21}N_3O_2$ • $CF_3COOH$ **FW:** 449.2 **Purity:** ≥95%

A crystalline solid **Stability:** ≥2 years at -20°C

**Summary:** Potent HDAC6 inhibitor ($IC_{50}$ = 15 nM) with 1,000-fold selectivity against all other HDAC isoforms ($IC_{50}$s >16 µM), excluding HDAC8 ($IC_{50}$ = 0.9 µM); induces α-tubulin hyperacetylation at 2.5 µM in primary cortical neuron cultures; displays dose-dependent neuronal protection of primary cortical neuron cultures at 5-10 µM

500 µg
1 mg
5 mg
10 mg




## Valproic Acid (sodium salt) 13033

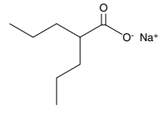
*[1069-66-5] 2-Propylvaleric Acid, Sodium Valproate*

**MF:** $C_8H_{15}O_2$ • Na **FW:** 166.2 **Purity:** ≥95%

A crystalline solid **Stability:** ≥2 years at -20°C

**Summary:** An analog of valeric acid, long used as an anti-convulsant; inhibits Class I HDACs with an $IC_{50}$ value of ~ 2 mM; also inhibits GSK3 and depletes cellular 1,4,5-$IP_3$

10 g
25 g
50 g
100 g



# Acetyl Readers

## Antibodies



## Biochemicals



## Kits



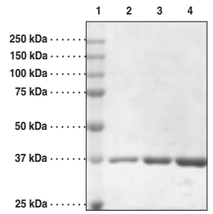
## Proteins



### BAZ2B bromodomain (human recombinant) 11917

*Bromodomain Adjacent to Zinc Finger Domain 2B, KIAA1476, WALp4*
**$M_r$:** 40.2 kDa **Purity:** ≥80% **Stability:** ≥1 year at -80°C
**Source:** Recombinant N-terminal GST-tagged protein consisting of amino acids 2,064-2,168 expressed in *E. coli* • BAZ2B is expressed in heart, skeletal, testis, and pancreatic tissues. A rare allele of BAZ2B has been identified to be a predictor of Sudden Cardiac Death. The full-length protein contains several DNA-targeting domains, including a methyl-CpG binding domain, a DNA-binding DDT domain, and a tandem PHD-bromodomain.

25 µg
50 µg
100 µg

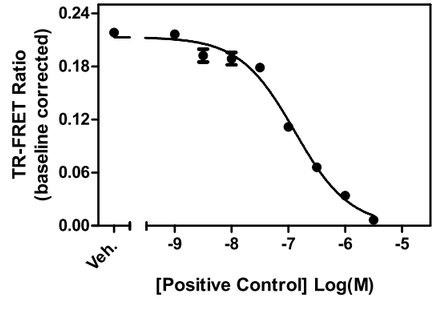


Lane 1: MW Markers
Lane 2: BAZ2B (2 µg)
Lane 3: BAZ2B (4 µg)
Lane 4: BAZ2B (8 µg)

### BAZ2B bromodomain TR-FRET Assay Kit 600710

*Bromodomain Adjacent to Zinc Finger Domain 2B, KIAA1476, WALp4*
**Stability:** ≥6 months at -80°C **Z' Factor:** 0.6
**Summary:** BAZ2B is a novel bromodomain-containing protein whose biological function, while not yet confirmed, is believed to function similar to ACF1, the *Drosophila* BAZ2B ortholog. ACF complexes play a role in establishing regular nucleosome spacing during chromatin assembly and influencing different remodeling outcomes at target loci. Cayman's BAZ2B bromodomain TR-FRET Assay Kit is a homogeneous, TR-FRET assay method amenable to rapid characterization of inhibitors of bromodomain/acetylated peptide interaction in a high throughput format.

384 wells
1,920 wells
9,600 wells

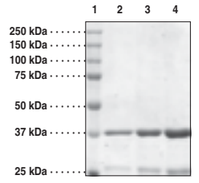





### BPTF bromodomain (human recombinant) 11918

*Bromodomain PHD Finger Transcription Factor*
**$M_r$:** 40.1 kDa **Purity:** ≥80% **Stability:** ≥1 year at -80°C
**Source:** Recombinant N-terminal GST-tagged protein consisting of amino acids 2,796-2,907 expressed in *E. coli* • BPTF is the largest component of the NURF chromatin remodeling complex. It includes adjacent PHD and bromodomains which recognize trimethylation of H3K4 or acetylation of lysines in histone 4, respectively. BPTF is an essential regulator of gene expression in early mouse embryo.

25 µg
50 µg
100 µg

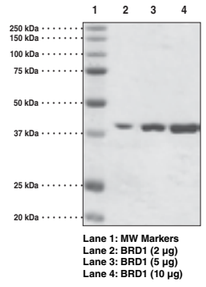


Lane 1: MW Markers
Lane 2: BPTF (2 µg)
Lane 3: BPTF (4 µg)
Lane 4: BPTF (8 µg)

### BRD1 bromodomain (human recombinant) 11507

*BR140-like protein, BRL, Bromodomain and PHD finger-containing protein 2, Bromodomain containing 1, BRPF1, BRPF2, DKFZp686F0325*
**$M_r$:** 41.1 kDa **Purity:** ≥95% **Stability:** ≥1 year at -80°C
**Source:** Recombinant N-terminal GST-tagged protein consisting of amino acids 556-680 expressed in *E. coli* • BRD1 is a bromodomain containing protein that has been identified as a susceptibility gene in neurological disorders, such as schizophrenia and bipolar affective disorder.

25 µg
50 µg
100 µg

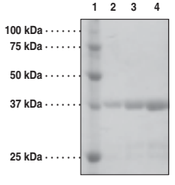


Lane 1: MW Markers
Lane 2: BRD1 (2 µg)
Lane 3: BRD1 (5 µg)
Lane 4: BRD1 (10 µg)

### BRD2 bromodomain 1 (human recombinant; GST-tagged) 11071

*Bromodomain containing 2, RING3, RNF3*
**$M_r$:** 42.4 kDa **Purity:** ≥95% **Stability:** ≥6 months at -80°C
**Source:** Recombinant N-terminal GST-tagged protein consisting of amino acids 65-187 expressed in *E. coli* • The isolated individual or tandem bromodomains of BRD2 have been shown to bind acetylated histone tails, serving to couple histone acetylation marks to the transcriptional regulation of target promoters.

25 µg
50 µg
100 µg

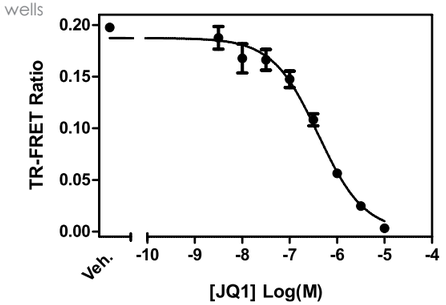


Lane 1: MW Markers
Lane 2: BRD2 Domain 1-GST (1 µg)
Lane 3: BRD2 Domain 1-GST (2 µg)
Lane 4: BRD2 Domain 1-GST (4 µg)

### BRD2 bromodomain 1 TR-FRET Assay Kit 600500

*Bromodomain containing 2, RING3, RNF3*
**Stability:** ≥6 months at -80°C **Z' Factor:** 0.71
**Summary:** The isolated individual or tandem bromodomains of BRD2 bind acetylated histone tails, which couples histone acetylation marks to the transcriptional regulation of target promoters. Small molecule inhibitors of bromodomain interactions hold promise as useful therapeutics for human disease. Cayman's BRD2 Bromodomain 1 TR-FRET Assay Kit is a homogeneous, TR-FRET assay method amenable to rapid characterization of inhibitors of bromodomain/acetylated peptide interaction in a high throughput format.

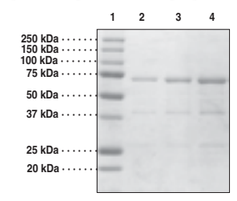
384 wells
1,920 wells
9,600 wells




### BRD2 bromodomain 1 and 2 (human recombinant) 11069

*Bromodomain containing 2, RING3, RNF3*
**$M_r$:** 71.2 kDa **Purity:** ≥90% **Stability:** ≥6 months at -80°C
**Source:** Recombinant GST-tagged protein consisting of amino acids 65-459 expressed in *E. coli* • The isolated individual or tandem bromodomains of BRD2 have been shown to bind acetylated histone tails, serving to couple histone acetylation marks to the transcriptional regulation of target promoters.

25 µg
50 µg
100 µg

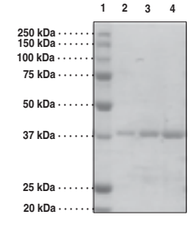


Lane 1: MW Markers
Lane 2: BRD2 Domain 1 and 2 (1.0 µg)
Lane 3: BRD2 Domain 1 and 2 (2.0 µg)
Lane 4: BRD2 Domain 1 and 2 (4.0 µg)

### BRD2 bromodomain 2 (human recombinant; GST tagged) 11070

*Bromodomain containing 2, RING3, RNF3*
**$M_r$:** 42 kDa **Purity:** ≥95% **Stability:** ≥6 months at -80°C
**Source:** Recombinant N-terminal GST-tagged protein consisting of amino acids 339-459 expressed in *E. coli* • The isolated individual or tandem bromodomains of BRD2 have been shown to bind acetylated histone tails, serving to couple histone acetylation marks to the transcriptional regulation of target promoters.

25 µg
50 µg
100 µg



Lane 1: MW Markers
Lane 2: BRD2 Domain 2-GST (1 µg)
Lane 3: BRD2 Domain 2-GST (2 µg)
Lane 4: BRD2 Domain 2-GST (4 µg)

# Bromodomains, ChromoHub, & STRING

by [Thomas G. Brock, Ph.D.]



In the everyday parlance of students of epigenetics, the enzymes that put marks on histones, like acetyltransferases, are 'writers', while those that remove the marks are 'erasers'. In keeping with the literary motif, the proteins that interact with the marks are called 'readers'. Bromodomains (BRDs) are the modules on certain proteins which act as the readers of ε-N-lysine acetylation marks placed on histones as well as other proteins. Proteins containing BRDs, and their co-regulators, are involved in chromatin remodeling, modulation of transcription, and cell signaling.[1] Dysfunction involving BRDs has been implicated in broad categories of diseases, including cancer, obesity, type 2 diabetes, and inflammation.[2,3] Examples of more specific diseases associated with mutations or fusions of genes expressing proteins with BRDs are veno-occlusive disease with immunodeficiency syndrome (SP110), X-linked mental retardation (BRWD3), and infant pro-B acute lymphoblastic leukemia (MLL).[4-6] Thus, these domains, proteins, and interacting complexes are of great interest. This brief article introduces BRDs, as well as some resources that are useful for their study.

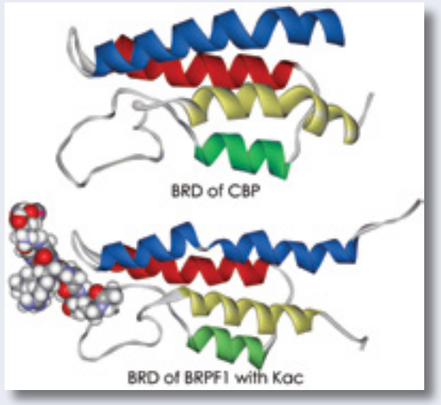



**Figure 1.** The structures of the BRDs of CBP and BRPF1, the latter bound to acetylated lysine (Kac), reveal a common overall structure. From 3DWY1 and 2RS9 in RCSB Protein Data Bank

## Bromodomains

In 1992, John Tamkun, a young scientist studying gene regulation in *Drosophila* with James Kennison and others, described a new gene involved in the transcriptional activation of homeotic genes, which they named brahma after the prominent Hindu god.[7] They noted that brahma contained a 77 amino acid (aa) motif which is found in other *Drosophila*, yeast, and human regulatory proteins, suggesting that this pattern may be characteristic of a new family of regulatory proteins. Now, over 20 years later, these BRDs are indeed known to be distinguishing features of several transcriptional regulators. However, they are also found on proteins that are not directly involved in gene transcription, including acetyltransferases and chromatin remodeling factors.[1] Just as Brahma has four heads, the domains named after him typically consist of four helices (Figure 1). Two loops, one long and the other short, bind the acetylated lysine. The presentation of BRDs on this scale may be misleading. Proteins which contain BRDs range from 807 to 2,969 amino acids, averaging about 1,500 amino acids. Given that histones are ~ 130 amino acids, a protein binding a histone using a BRD is like a person, averaging 150 lbs but ranging up to 296 lbs, biting a 13 lb turkey at a Thanksgiving dinner.

Of course, the BRD/acetylated lysine association is more of a lock and key interaction than mouth on drumstick. Some histone acetylation sites are very specific in which proteins can bind to them, while others are more promiscuous.[1] Similarly, proteins vary in how specific they are for acetylation sites. In addition, recent evidence indicates that neighboring posttranslational modifications, such as acetylation and phosphorylation, affect binding. That is, BRDs recognize patterns of marks on histones. For example, the combination of acetylation on H3K9 and H4K16 with phosphorylation at H3S10 provides the requisites for BRD4 binding, recruitment of TEFb, and gene transcription.[8] The recruitment of partner proteins is an important element in signaling through BRDs. This topic raises the questions: where can one find information about these interactions, how important are they, and what is their impact?

## ChromoHub

ChromoHub(http://apps.thesgc.org/resources/phylogenetic_trees/index.php) is a data hub for navigators of chromatin-mediated signaling.[9] Developed by researchers at the Structural Genomics Consortium at the University of Toronto, this site is a valuable resource for anyone trying to keep up with research related to chromatin-mediated regulation of epigenetic mechanisms. It initially segregates data according to 19 different domains involved in writing, reading, or erasing histone marks, generating phylogenetic trees which are either gene-based, produced using ClustalW, or domain-based, developed from seed sequence alignments using ICM. These trees are then overlaid with the information of interest to the user.

The first option listed in ChromoHub refers to Disease Associations and provides references for each protein indicating involvement in inflammation, cancer, viral infections, neurological diseases, metabolic disorders, immune disorders, or regenerative medicine. Perhaps not surprisingly, BRD-containing proteins have been predominantly linked with cancer. This may in part reflect low-hanging fruit, since associating chromatin remodeling proteins to cancer is easier than identifying more specific roles for each protein. Several additional options are available at ChromoHub to extend the information related to cancer and provide quality information. For example, evaluation of gene fusions in cancer shows that there is abundant evidence for fusions of MYST histone acetyltransferases with CBP in leukemias. PBRM1 shows the highest rate of somatic mutations in cancer, found in 16% of 288 patients with kidney renal clear cell carcinoma. Of course, these cancer links will be useful for all of the chromatin-modifying proteins.

Moving beyond the disease links, a user might choose options regarding funding and "jump in activity" to evaluate which BRD-containing proteins have been of greatest recent interest. ChromoHub shows that proteins like CECR2 and PBRM1 have shown upswings in interest during the past year (Figure 2). The funding option also provides publications for each protein, segregated by year. According to abstracts provided by ChromoHub, ATAD2 has been identified as a predictor of poor prognosis in breast and lung cancers, helping to explain a jump in funding for ATAD2 research in 2012. ChromoHub also indicates that BAZ2B is drawing interest for its documented link with sudden cardiac death, while money to study CECR2 is going to a computational biologist to do an evolutionary analysis of protein superfamilies. By using options like these, a scientist can find recent information specifically about each protein and begin to understand where interests in the field of chromatin remodeling are changing.

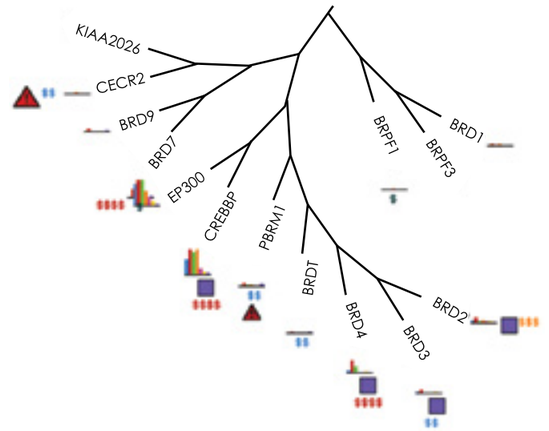



**Figure 2.**
A partial presentation of a ChromoHub BRD tree shows where information is available regarding disease associations (graphs), inhibitors (purple boxes), funding (dollar signs), and recent jump in activity (red triangle) for some proteins with BRDs. Hovering over a symbol opens a link to annotated information.

## STRING 9.0

Like a scientist who leverages teamwork to accomplish great things, proteins with BRDs work with other proteins to achieve their goals. In ChromoHub, the option called 'protein interactions' allows one to interrogate potential partners for each protein, using the application STRING.[10] For example, the BRD and PHD finger-containing protein 1, BRPF1, links to several proteins by varying degrees (Figure 3). Different colored lines indicate different evidence supporting the relationship, with red lines indicating experimentation, blue lines for databases, and green lines for textmining; other criteria also exist. Correlation scores are also provided, as well as basic information about each of the proteins. A quick examination of this page provides the bottom line: BRPF1 is a component of a complex that also contains MYST3 (aka MOZ, KAT6A), MEAF6, MYST4 (aka MORF, KAT6B), and ING5. Additional information on the page says that BRPF1 is a "component of the MOZ/MORF complex which has a histone H3 acetyltransferase activity" and that it "positively regulates the transcription of RUNX1 and RUNX2." In short, STRING provides enough information for an inquisitive scientist to begin to understand the actions of any given chromatin-modifying protein.

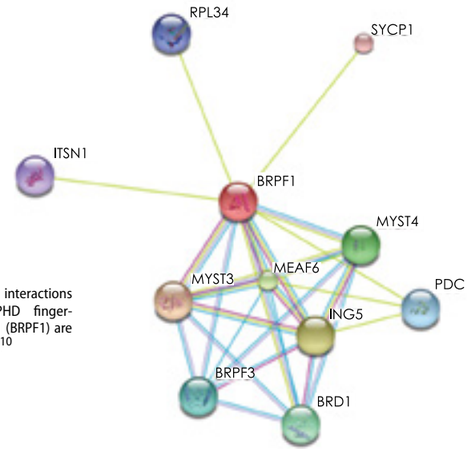



**Figure 3.**
Potential protein interactions with BRD and PHD finger-containing protein 1 (BRPF1) are given by STRING 9.0.[10]

Of course, STRING has limitations. The proteins linked to BRPF1 by textmining only (green lines) merely appear in the same abstract together. Thus, BRPF1 and intersectin 1 (ITSN1) are both substrates of granzyme B, while BRPF1 and synaptonemal complex protein 1 (SYCP1) genes are regulated by hydrogen peroxide. These kinds of associations redefine the meaning of 'protein interactions', and not in a favorable way. On the upside, the website is updated every two years. STRING 9.0 was generated in 2011, which means that STRING 9.1 is due out soon. In fact, a preview version of STRING 9.1 reveals that BRPF1, with the MOZ/MORF complex, associates with its target histone H3, and associations with ITSN1 and SYCP1 are no longer listed (although new tenuous associations with a collagen protein, COL4A3, and a demethylase, JMJD1C, are added). Liberally speaking, STRING errs on the side of giving extra information.

## Cayman Chemical

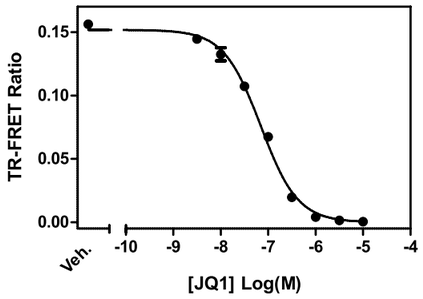
Perhaps the best source for products and services that you can actually use to advance your research is Cayman, which has a dedicated team of scientists studying epigenetics with an emphasis on BRDs. They have engineered a large collection of human recombinant BRDs, synthesized inhibitors, and developed assays to screen for novel modulators of BRD/acetyllysine binding. Most of these products are listed in the Acetyl Readers section of this catalog.

For article references see **page 64**

## BRD2 bromodomain 2 TR-FRET Assay Kit 600510

*Bromodomain containing 2, RING3, RNF3*
**Stability:** ≥6 months at -80°C **Z' Factor:** 0.82
**Summary:** The isolated individual or tandem bromodomains of BRD2 bind acetylated histone tails, which couples histone acetylation marks to the transcriptional regulation of target promoters. Small molecule inhibitors of bromodomain interactions hold promise as useful therapeutics for human disease. Cayman's BRD2 Bromodomain 2 TR-FRET Assay Kit is a homogeneous, TR-FRET assay method amenable to rapid characterization of inhibitors of bromodomain/acetylated peptide interaction in a high throughput format.

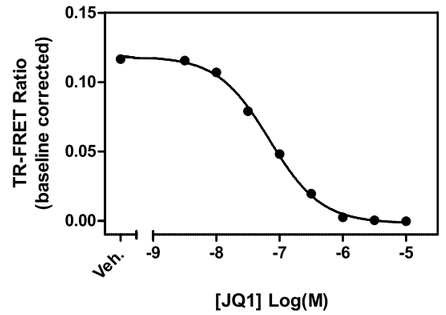
384 wells
1,920 wells
9,600 wells




## BRD3 bromodomain 1 TR-FRET Assay Kit 600630

*Bromodomain containing protein 3, ORFX, RING3L, RING3-like protein*
**Stability:** ≥6 months at -80°C **Z' Factor:** 0.86
**Summary:** The isolated individual or tandem bromodomains of many BET family members, including BRD2, BRD3, BRD4, and BRDT, bind acetylated histone tails, serving to couple histone acetylation marks to the transcriptional regulation of target promoters. Small molecule inhibitors of bromodomain interactions hold promise as useful therapeutics for human disease. Cayman's BRD3 bromodomain 1 TR-FRET Assay Kit is a homogeneous, TR-FRET assay method amenable to rapid characterization of inhibitors of bromodomain/acetylated peptide interaction in a high throughput format.

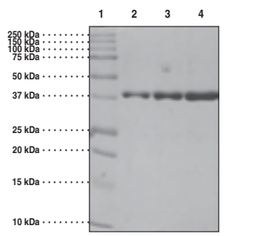
384 wells
1,920 wells
9,600 wells




## BRD3 bromodomain 1 (human recombinant) 11285

*Bromodomain containing protein 3, ORFX, RING3L, RING3-like protein*
**$M_r$:** 41.2 kDa **Purity:** ≥95% **Stability:** ≥1 year at -80°C
**Source:** Recombinant N-terminal GST-tagged protein consisting of amino acids 24-144 expressed in *E. coli* • The isolated individual or tandem bromodomains of BRD3 have been shown to bind acetylated histone tails, serving to couple histone acetylation marks to the transcriptional regulation of target promoters.

25 µg
50 µg
100 µg

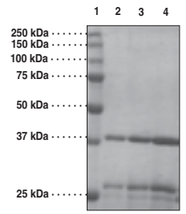



Lane 1: MW Markers
Lane 2: BRD3 bromodomain 1 (2 µg)
Lane 3: BRD3 bromodomain 1 (5 µg)
Lane 4: BRD3 bromodomain 1 (10 µg)

## BRD4 bromodomain 1 (human recombinant; GST tagged) 11068

*Bromodomain containing 4, HUNK1, MCAP*
**$M_r$:** 41.4 kDa **Purity:** ≥60% **Stability:** ≥6 months at -80°C
**Source:** Recombinant N-terminal GST-tagged protein consisting of amino acids 49-170 expressed in *E. coli* • The isolated individual or tandem bromodomains of BRD4 have been shown to bind acetylated histone tails, serving to couple histone acetylation marks to the transcriptional regulation of target promoters.

25 µg
50 µg
100 µg




Lane 1: MW Markers
Lane 2: BRD4 Domain 1-GST (1 µg)
Lane 3: BRD4 Domain 1-GST (2 µg)
Lane 4: BRD4 Domain 1-GST (4 µg)

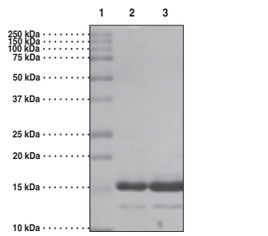




## BRD4 bromodomain 1 (human recombinant; His-tagged) 11720

*Bromodomain containing 4, HUNK1, MCAP*
**$M_r$:** 16.6 kDa **Purity:** ≥95% **Stability:** ≥6 months at -80°C
**Source:** Recombinant N-terminal His-tagged protein consisting of amino acids 49-170 expressed in *E. coli* • The isolated individual or tandem bromodomains of BRD4 have been shown to bind acetylated histone tails, serving to couple histone acetylation marks to the transcriptional regulation of target promoters.

25 µg
50 µg
100 µg

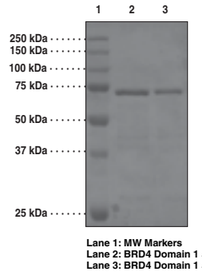



Lane 1: MW Markers
Lane 2: BRD4 bromodomain 1 (5 µg)
Lane 3: BRD4 bromodomain 1 (10 µg)

## BRD4 bromodomain 1 and 2 (human recombinant) 11052

*Bromodomain containing 4, HUNK1, MCAP*
**$M_r$:** 73.4 kDa **Purity:** ≥90% **Stability:** ≥6 months at -80°C
**Source:** Recombinant GST-tagged protein consisting of amino acids 49-460 expressed in *E. coli* • The isolated individual or tandem bromodomains of BRD4 have been shown to bind acetylated histone tails, serving to couple histone acetylation marks to the transcriptional regulation of target promoters.

25 µg
50 µg
100 µg

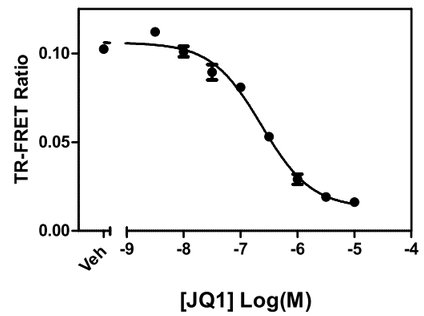



Lane 1: MW Markers
Lane 2: BRD4 Domain 1 and 2 (5.0 µg)
Lane 3: BRD4 Domain 1 and 2 (2.5 µg)

## BRD4 bromodomain 1 TR-FRET Assay Kit 600520

*Bromodomain containing 4, HUNK1, MCAP*
**Stability:** ≥6 months at -80°C **Z' Factor:** 0.73
**Summary:** The isolated individual or tandem bromodomains of BRD4 bind acetylated histone tails, which couples histone acetylation marks to the transcriptional regulation of target promoters. Small molecule inhibitors of bromodomain interactions hold promise as useful therapeutics for human disease. Cayman's BRD4 bromodomain 1 TR-FRET Assay Kit is a homogeneous, TR-FRET assay method amenable to rapid characterization of inhibitors of bromodomain/acetylated peptide interaction in a high throughput format.

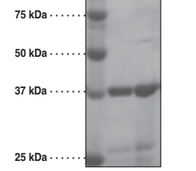
384 wells
1,920 wells
9,600 wells




## BRD4 bromodomain 2 (human recombinant; GST-tagged) 11066

*Bromodomain containing 4, HUNK1, MCAP*
**$M_r$:** 40.6 kDa **Purity:** ≥95% **Stability:** ≥6 months at -80°C
**Source:** Recombinant N-terminal GST-tagged protein consisting of amino acids 342-460 expressed in *E. coli* • The isolated individual or tandem bromodomains of BRD4 have been shown to bind acetylated histone tails, serving to couple histone acetylation marks to the transcriptional regulation of target promoters.

25 µg
50 µg
100 µg

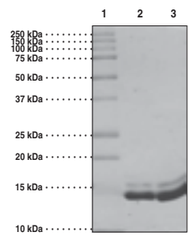



Lane 1: MW Markers
Lane 2: BRD4 Domain 2-GST (1 µg)
Lane 3: BRD4 Domain 2-GST (2 µg)

## BRD4 bromodomain 2 (human recombinant; His-tagged) 11721

*Bromodomain containing 4, HUNK1, MCAP*
**$M_r$:** 15.8 kDa **Purity:** ≥95% **Stability:** ≥6 months at -80°C
**Source:** Recombinant N-terminal His-tagged protein consisting of amino acids 342-460 expressed in *E. coli* • The isolated individual or tandem bromodomains of BRD4 have been shown to bind acetylated histone tails, serving to couple histone acetylation marks to the transcriptional regulation of target promoters.

25 µg
50 µg
100 µg

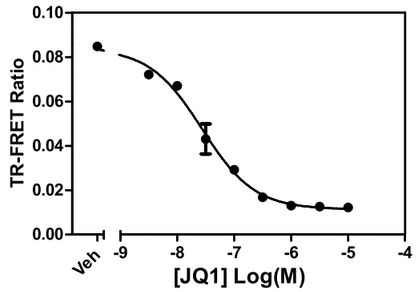



Lane 1: MW Markers
Lane 2: BRD4 bromodomain 2 (5 µg)
Lane 3: BRD4 bromodomain 2 (10 µg)

## BRD4 bromodomain 2 TR-FRET Assay Kit 600530

*Bromodomain containing 4, HUNK1, MCAP*
**Stability:** ≥6 months at -80°C **Z' Factor:** 0.68
**Summary:** The isolated individual or tandem bromodomains of BRD4 bind acetylated histone tails, which couples histone acetylation marks to the transcriptional regulation of target promoters. Small molecule inhibitors of bromodomain interactions hold promise as useful therapeutics for human disease. Cayman's BRD4 Bromodomain 2 TR-FRET Assay Kit is a homogeneous, TR-FRET assay method amenable to rapid characterization of inhibitors of bromodomain/acetylated peptide interaction in a high throughput format.

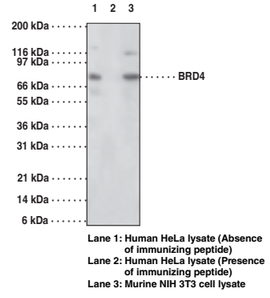
384 wells
1,920 wells
9,600 wells




## BRD4/HUNK1 Polyclonal Antibody 13497

*Bromodomain containing 4*
Protein G-purified IgG **Stability:** ≥1 year at -80°C
**Summary:** Antigen: peptide from human BRD4 within the region of amino acids 150-200 • Host: rabbit • Cross Reactivity:(+) chimpanzee, human, mouse, and rat BRD4 • Application(s): WB • BRD4 is a chromatin-binding protein whose expression is induced in response to growth stimuli. It acts at different stages of the cell cycle to regulate cell growth and chromosomal dynamics during mitosis.

1 ea

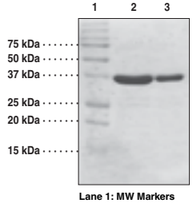


Lane 1: Human HeLa lysate (Absence of immunizing peptide)
Lane 2: Human HeLa lysate (Presence of immunizing peptide)
Lane 3: Murine NIH 3T3 cell lysate

## BRD9 bromodomain (human recombinant) 11509

*Bromodomain containing 9*
**$M_r$:** 40.7 kDa **Purity:** ≥95% **Stability:** ≥1 year at -80°C
**Source:** Recombinant N-terminal GST-tagged protein consisting of amino acids 21-137 expressed in *E. coli* • Human BRD9 contains a single bromodomain and has five isoforms that are produced by alternative splicing.

25 µg
50 µg
100 µg

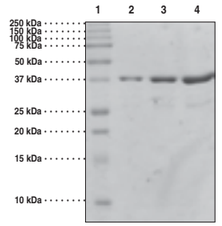


Lane 1: MW Markers
Lane 2: BRD9 (20 µg)
Lane 3: BRD9 (7.5 µg)

## BRDT bromodomain 1 (human recombinant) 11548

*BRD6, BRD-containing protein testis specific, Cancer/testis antigen 9, CT9, RING3-like protein*
**$M_r$:** 40.6 kDa **Purity:** ≥95% **Stability:** ≥1 year at -80°C
**Source:** Recombinant N-terminal GST-tagged protein consisting of amino acids 21-137 expressed in *E. coli* • BRDT is similar to the RING3 protein family and possesses 2 bromodomain motifs and a PEST sequence motif, which is a region rich in proline (P), glutamic acid (E), serine (S), and threonine (T) residues known to have a short intracellular half-life.

25 µg
50 µg
100 µg

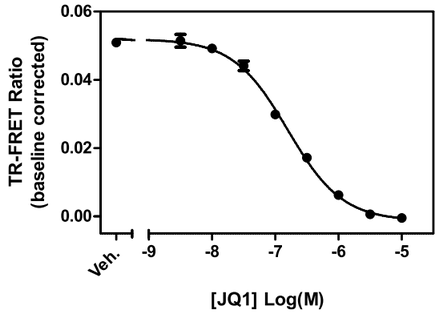


Lane 1: MW Markers
Lane 2: BRDT (2 µg)
Lane 3: BRDT (5 µg)
Lane 4: BRDT (10 µg)

## BRDT bromodomain 1 TR-FRET Assay Kit 600650

*BRD6, BRD-containing protein testis specific, Cancer/testis antigen 9, CT9, RING3-like protein*
**Stability:** ≥6 months at -80°C **Z' Factor:** 0.82
**Summary:** The isolated individual or tandem bromodomains of many BET family members, including BRD2, BRD3, BRD4, and BRDT, bind acetylated histone tails, serving to couple histone acetylation marks to the transcriptional regulation of target promoters. Small molecule inhibitors of bromodomain interactions hold promise as useful therapeutics for human disease. Cayman's BRDT Bromodomain 1 TR-FRET Assay Kit is a homogeneous, TR-FRET assay method amenable to rapid characterization of inhibitors of bromodomain/acetylated peptide interaction in a high throughput format.

384 wells
1,920 wells
9,600 wells



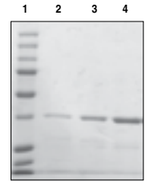





## BRDT bromodomain 2 (human recombinant) 11649

*BRD6, Bromodomain testis-specific protein, Cancer/testis antigen 9, CT9, RING3-like protein*
**$M_r$:** 41.2 kDa **Purity:** ≥95% **Stability:** ≥1 year at -80°C
**Source:** Recombinant N-terminal GST-tagged protein consisting of amino acids 259-379 expressed in *E. coli* • BRDT shares homology with the RING3 protein. The two bromodomains of BRDT recognize acetylated histone H4. Loss of BRDT leads to defects in spermatogenesis. In addition to testis specific expression, BRDT was found in approximately 20% of non-small cell lung cancers.

25 µg
50 µg
100 µg

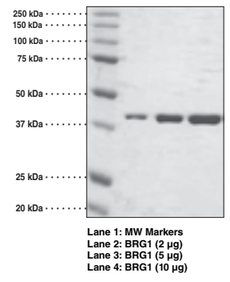


Lane 1: MW Markers
Lane 2: BRDT bd 2 (1 µg)
Lane 3: BRDT bd 2 (2 µg)
Lane 4: BRDT bd 2 (4 µg)

## BRG1 bromodomain (human recombinant) 11284

*ATP-dependent helicase SMARCA4, BAF190A Mitotic growth and transcription activator, BRG1-associated factor 190A, Protein BRG-1*
**$M_r$:** 41.8 kDa **Purity:** ≥95% **Stability:** ≥1 year at -80°C
**Source:** Recombinant N-terminal GST-tagged protein consisting of amino acids 1,448-1,575 expressed in *E. coli* • BRG1 is a member of the SWI/SNF protein family, which forms part of a large ATP-dependent chromatin remodeling complex. BRG1 is mutated in many cancer cell lines, such as breast, prostate, lung, pancreas and colon. Further, BRG1 has an important role as a tumor suppressor.

25 µg
50 µg
100 µg

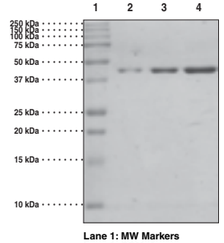


Lane 1: MW Markers
Lane 2: BRG1 (2 µg)
Lane 3: BRG1 (5 µg)
Lane 4: BRG1 (10 µg)

## BRM bromodomain (human recombinant) 11289

*SMARCA2A/B, SWI/SNF ATPase*
**$M_r$:** 43.7 kDa **Purity:** ≥95% **Stability:** ≥1 year at -80°C
**Source:** Recombinant N-terminal GST-tagged protein consisting of amino acids 1,367-1,511 expressed in *E. coli* • BRM is a member of the SWI/SNF protein family, which forms part of a large ATP-dependent chromatin remodeling complex. This complex is required for transcriptional activation of genes normally repressed by chromatin.

25 µg
50 µg
100 µg

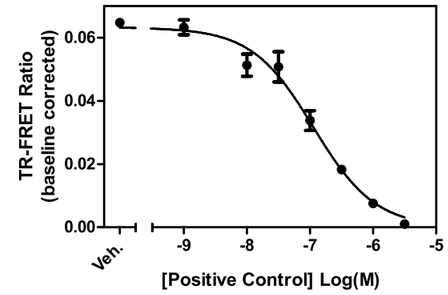


Lane 1: MW Markers
Lane 2: BRM (2 µg)
Lane 3: BRM (5 µg)
Lane 4: BRM (10 µg)

## BRM bromodomain TR-FRET Assay Kit 600730

**Stability:** ≥6 months at -80°C **Z' Factor:** 0.62
**Summary:** The SWI/SNF family of ATP-dependent chromatin remodeling enzymes catalyzes structural changes that allow proteins to access the nucleosomal DNA, alter the position of the nucleosomes on the DNA, or eject the histone octamer from the template. Mammalian SWI/SNF remodelers contain either BRM (SMARCA2) or BRG1 (SMARCA4) as their catalytic subunit. These subunits also contain a C-terminal bromodomain that binds to acetylated residues on histone tails. Small molecule inhibitors of BRM interactions with peptide binding partners hold promise as useful therapeutics for human disease. Cayman's BRM bromodomain TR-FRET Assay Kit is a homogeneous, TR-FRET assay method amenable to rapid characterization of inhibitors of bromodomain/acetylated peptide interaction in a high throughput format.

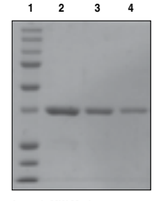
384 wells
1,920 wells
9,600 wells




## BRPF3 bromodomain 1 (human recombinant) 11650

*Bromodomain and PHD Finger Containing 3, KIAA1286, MGC 58603*
**$M_r$:** 41.2 kDa **Purity:** ≥95% **Stability:** ≥1 year at -80°C
**Source:** Recombinant N-terminal GST-tagged protein consisting of amino acids 576-701 expressed in *E. coli* • BRPF3 is a component of the MOZ/MORF HAT complex. The addition of BRPF proteins to MOZ/MORF increases its HAT activity. Consequently, BRPF3 is likely to play a role in regulation of transcriptional activation by MOZ/MORF.

25 µg
50 µg
100 µg

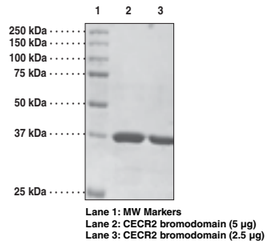


Lane 1: MW Markers
Lane 2: BRPF3 (8 µg)
Lane 3: BRPF3 (4 µg)
Lane 4: BRPF3 (2 µg)

## CECR2 bromodomain (human recombinant) 14133

*Cat Eye Syndrome Critical Region Protein 2*
**$M_r$:** 40.6 kDa **Purity:** ≥95% **Stability:** ≥1 year at -80°C
**Source:** Recombinant N-terminal GST-tagged protein consisting of amino acids 424-538 expressed in *E. coli* • CECR2 is a transcription factor that forms a heterodimeric complex with CECR2-containing-remodeling factor (CERF). The CECR2/CERF forms a complex with the ATP-dependent chromatin remodeler SNF2L playing a critical role in neurulation. More recently, the bromodomain of CECR2 was shown to have strong γ-H2AX inhibition activity suggesting that CECR2 may play a role in DNA damage response.

25 µg
50 µg
100 µg

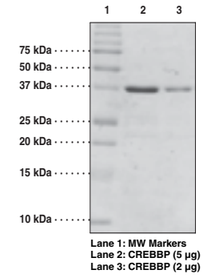


Lane 1: MW Markers
Lane 2: CECR2 bromodomain (5 µg)
Lane 3: CECR2 bromodomain (2.5 µg)

## CREB-binding protein bromodomain (human recombinant) 11288

*cAMP-responsive element-binding protein 1 CREB-1, CBP, CREBBP*
**$M_r$:** 40.8 kDa **Purity:** ≥95% **Stability:** ≥1 year at -80°C
**Source:** Recombinant N-terminal GST-tagged protein consisting of amino acids 1,081-1,197 expressed in *E. coli* • CREBBP bromodomain has been shown to modulate the stability and function of the tumor suppressor protein p53. CREBBP bromodomain recognizes the acetylated lysine residue 382 on p53.

25 µg
50 µg
100 µg

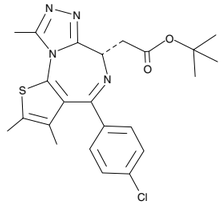


Lane 1: MW Markers
Lane 2: CREBBP (5 µg)
Lane 3: CREBBP (2 µg)

## (+)-JQ1 11187

*[1268524-70-4]*
**MF:** $C_{23}H_{25}ClN_4O_2S$ **FW:** 457.0 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** Displaces BET proteins from chromatin by competitively binding to the acetyl-lysine recognition pocket of BET bromodomains; binds BRD4 bromodomains 1 and 2 with $K_d$ values of ~ 50 and 90 nM, respectively

1 mg
5 mg
10 mg

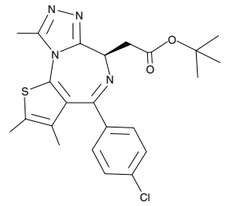



*NOTE: Manufactured, marketed, and sold with authorization from Tensha Therapeutics, Inc. Patent Pending relating to PCT Publ. No. WO/2011/143669, and any related U.S. and foreign patents and patent applications.*

## (-)-JQ1 11232

*[1268524-71-5]*
**MF:** $C_{23}H_{25}ClN_4O_2S$ **FW:** 457.0 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** The inactive stereoisomer of a selective BET bromodomain inhibitor

1 mg
5 mg
10 mg

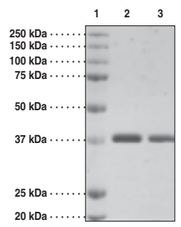



*NOTE: Manufactured, marketed, and sold with authorization from Tensha Therapeutics, Inc. Patent Pending relating to PCT Publ. No. WO/2011/143669, and any related U.S. and foreign patents and patent applications.*

## PCAF bromodomain (human recombinant) 11920

*KAT2B, p300/CBP-associated factor*
**$M_r$:** 40.9 kDa **Purity:** ≥95% **Stability:** ≥6 months at -80°C
**Source:** Recombinant N-terminal GST-tagged protein consisting of amino acids 714-831 expressed in *E. coli* • PCAF is a transcriptional coactivator that works both as a histone lysine acetyltransferase, through its HAT domain, and as an acetyl-lysine reader through its conserved bromodomain located directly C-terminal to the HAT domain. The PCAF bromodomain binds acetylated histone H3 and H4 as well as non-histone targets. Bromodomain binding is dictated by the position of the acetylated lysine as well as interactions with specific residues flanking the acetyl-lysine.

25 µg
50 µg
100 µg

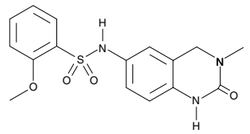


Lane 1: MW Markers
Lane 2: PCAF bromodomain (4 µg)
Lane 3: PCAF bromodomain (2 µg)

## PFI-1 11155

**MF:** $C_{16}H_{17}N_3O_4S$ **FW:** 347.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** A BET bromodomain inhibitor that exhibits inhibitory activity at BRD2 bromodomain 2 and BRD4 bromodomain 1 with $IC_{50}$ values of 98 nM and 0.22 µM, respectively

1 mg
5 mg
10 mg
25 mg



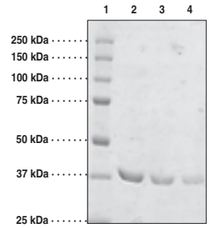





## Polybromo-1D bromodomain 1 (human recombinant) 11652

*BAF180, BRG1-associated factor 180, hPB1, MGC165155, MGC165156, PB1, PBRM1, Protein Polybromo-1*
**$M_r$:** 42.8 kDa **Purity:** ≥95% **Stability:** ≥1 year at -80°C
**Source:** Recombinant N-terminal GST-tagged protein consisting of amino acids 23-156 expressed in *E. coli* • PBRM1 contains six bromodomains and is a component of the SWI/SNF complex, PBAF. PBAF is targeted to acetylated sites in chromatin by the PBRM1 bromodomains, where it plays a role in cell cycle regulation and tumor suppression.

25 µg
50 µg
100 µg

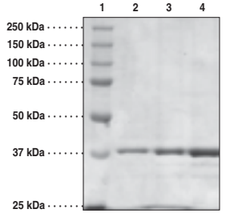


Lane 1: MW Markers
Lane 2: PBRM1 (8 µg)
Lane 3: PBRM1 (4 µg)
Lane 4: PBRM1 (2 µg)

## TAF1 bromodomain 1 (human recombinant) 11922

*BA2R, CCG1, CCGS, DYT3, KAT4, NSCL2, TAF1 RNA Polymerase II, TAFII250, TAF2A, TATA Box Binding Protein (TBP)-Associated Factor, XDP*
**$M_r$:** 41.7 kDa **Purity:** ≥95% **Stability:** ≥1 year at -80°C
**Source:** Recombinant N-terminal GST-tagged protein consisting of amino acids 1,371-1,496 expressed in *E. coli* • TAF1 is a component of transcription factor IID, and binds to core promoter sequences at the transcription start site. TAF1 helps control transcription by both its kinase and histone acetyltransferase enzymatic activities. It interacts with transcriptional activators such as the androgen receptor to promote transcription.

25 µg
50 µg
100 µg

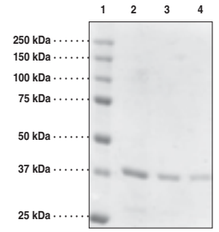


Lane 1: MW Markers
Lane 2: TAF1 (2 µg)
Lane 3: TAF1 (4 µg)
Lane 4: TAF1 (8 µg)

## TRIM24 bromodomain (human recombinant) 11653

*E3 Ubiquitin-protein Ligase TRIM24, hTIF1, PTC6, RING finger protein 82, RNF82, Transcriptional Intermediary Factor 1-α, Tripartite Motif Containing 24*
**$M_r$:** 40.9 kDa **Purity:** ≥95% **Stability:** ≥1 year at -80°C
**Source:** Recombinant N-terminal GST-tagged protein consisting of amino acids 896-1,014 expressed in *E. coli* • TRIM24 is a transcriptional cofactor, whose inactivation leads to hepatocellular carcinoma in mice. The N-terminal TRIM domain of TRIM24 binds ligand-bound nuclear receptors, while its tandem C-terminal plant homeo-domain and bromodomain target TRIM24 to acetylated histones in chromatin.

25 µg
50 µg
100 µg

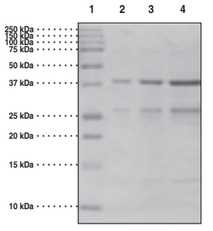


Lane 1: MW Markers
Lane 2: TRIM24 (8 µg)
Lane 3: TRIM24 (4 µg)
Lane 4: TRIM24 (2 µg)

## WDR9 bromodomain 2 (human recombinant) 11549

*BRD and WD repeat-containing protein 1, WD repeat-containing protein 9*
**$M_r$:** 40.3 kDa **Purity:** ≥85% **Stability:** ≥1 year at -80°C
**Source:** Recombinant N-terminal GST-tagged protein consisting of amino acids 1,310-1,426 expressed in *E. coli* • WDR9 possesses two bromodomain motifs and eight WD repeats. WDR9 is also known to interact with BRG1 (SMARCA4). This product contains the bromodomain 2 region of WDR9.

25 µg
50 µg
100 µg



Lane 1: MW Markers
Lane 2: WDR9 (2 µg)
Lane 3: WDR9 (5 µg)
Lane 4: WDR9 (10 µg)

*NOTE: SUMO Affinity tag used under license from LifeSenso*

*Cayman Chemical is helping make research possible with*

# Epigenetic Screening and Lead Discovery SERVICES

## Learn more

For more information or to receive a quote for contract services please contact our sales department at

**1-800-364-9897**
or email us at
**sales@caymanchem.com**

## Epigenetics Screening Library (96-Well) 11076

**10 mM solutions in DMSO Stability: ≥2 years at -20°C**
**Summary:** The Epigenetics Screening Library contains various molecules that are known to modulate the activity of a variety of epigenetic 'writers and erasers' and 'reader' proteins in a 96-well Matrix tube rack format as 10 mM stocks in DMSO.

It may include compounds that modulate the activity of methyltransferases, demethylases, histone acetyltransferases, histone deacetylases, and acetylated histone binding proteins. The composition of this screening library will always vary somewhat depending upon our inventory. Stability data is not available for compounds as supplied in the screening library.

**50 µl • 100 µl • 200 µl**

## Screening and Profiling Services

Cayman offers a dedicated Epigenetic Screening Laboratory designed to be flexible and innovative. High-throughput capabilities allow us to work with you to screen a chemical library against specific epigenetic targets. Alternatively, our broad collection of epigenetic enzymes, substrates, and assays enable profiling the activity of a few compounds against several targets. Our experienced staff and expanding suite of assays are designed to get the results you need in a timely manner.

- **Comprehensive screening laboratory focused on epigenetics**
- **Backed by Cayman's core strengths in protein production, assay development, chemical synthesis, and medicinal chemistry**
- **Capacity to test compounds at a rate of up to 100,000 compounds per week**
- **Ability to profile compounds against a broad epigenetic enzyme panel**

**Includes assays for:**

**methyltransferases**
**demethylases**
**acetyltransferases**
**deacetylases (HDACs and SIRTS)**
**histone code readers (*e.g.* bromodomain proteins)**

## Gene-to-Structure Services

Cayman Chemical has been making recombinant proteins and developing assays for many years. As an extension of these core competencies, we now offer full gene-to-structure contract services. Our experienced lab staff will clone, express, purify, and determine the structure of your protein in the presence or absence of ligands. We are fully equipped to aid you in the drug discovery process.

- **Custom and large scale protein production**
- **Macromolecular X-ray crystallography**
- **Biophysical characterization**
- **Structure Based Drug Design (SBDD)**

# Methyl **Readers**

## Antibodies



## Biochemicals



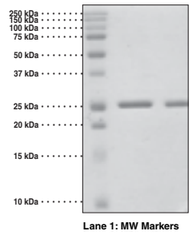
## Proteins



### HP1-α (human recombinant) 11235

*Antigen p25, CBX5, Chromobox Homolog 5, Heterochromatin Protein 1-α*
**$M_r$:** 24.1 kDa **Purity:** ≥95% **Stability:** ≥6 months at -80°C
**Source:** Recombinant N-terminal His-tagged protein consisting of amino acids 2-191 expressed in *E. coli* • HP1-α is involved in gene regulation and heterochromatin formation. The chromodomain of HP1-α has been shown to recognize di- and tri-methylated histone H3K9. The methyltransferase SETDB1 can then be recruited which performs H3K9 trimethylation, leading to chromatin condensation and gene silencing. The chromoshadow domain facilitates protein-protein interactions and is responsible for recruitment to sites of DNA damage, where HP1-α helps to reorganize chromatin as part of the DNA damage response system.

25 µg
50 µg
100 µg

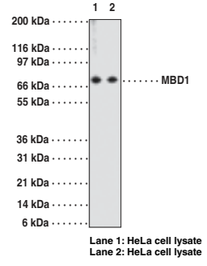


Lane 1: MW Markers
Lane 2: HP1-α (5 µg)
Lane 3: HP1-α (2.5 µg)

### MBD1 Monoclonal Antibody (Clone 100B272.1) 13771

*Methyl-CpG-Binding Domain 1*
Protein G-purified IgG **Stability:** ≥1 year at -20°C
**Summary:** Antigen: human MBD1 amino acids 391-405 • Host: mouse, clone 100B272.1 • Isotype: $IgG_1$ • Cross Reactivity: (+) human MBD1 • Application(s): WB • MBD1 contains an MBD that allows it to bind specifically to methylated DNA and to repress transcription from methylated gene promoters.

1 ea

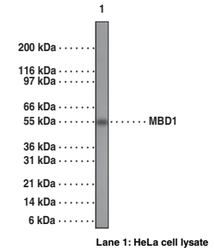


Lane 1: HeLa cell lysate
Lane 2: HeLa cell lysate

### MBD1 Polyclonal Antibody 13772

*Methyl-CpG-Binding Domain 1*
Protein G-purified IgG **Stability:** ≥1 year at -20°C
**Summary:** Antigen: human MBD1 amino acids 98-113 and 391-405 • Host: rabbit • Cross Reactivity: (+) human MBD1 • Application(s): WB • MBD1 contains an MBD that allows it to bind specifically to methylated DNA and to repress transcription from methylated gene promoters.

1 ea

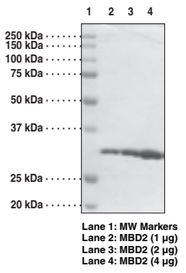


Lane 1: HeLa cell lysate

### MBD2 (human recombinant; methyl binding domain aa 150-220) 11286

*Methyl-CpG Binding Domain 2, Methyl Cytosine Binding Domain 2*
**$M_r$:** 34.8 kDa **Purity:** ≥95% **Stability:** ≥1 year at -80°C
**Source:** Recombinant N-terminal GST-tagged protein consisting of amino acids 150-220 expressed in *E. coli* • MBD2 specifically binds to methylated promoters on CpG islands. MBD2 binding to 5mC facilitates the recruitment of chromatin remodeling and transcriptional repressor complexes, which results in a repressive chromatin state.

25 µg
50 µg
100 µg

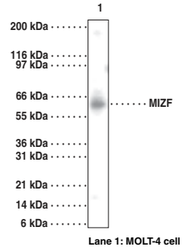


Lane 1: MW Markers
Lane 2: MBD2 (1 µg)
Lane 3: MBD2 (2 µg)
Lane 4: MBD2 (4 µg)

### MBD2 Binding Zinc Finger Polyclonal Antibody 13777

*HINFP, Histone H4 Trancription Factor, Methyl-CpG-Binding Domain 2, MIZF*
Protein G-purified IgG **Stability:** ≥1 year at -20°C
**Summary:** Antigen: human MIZF amino acids 180-194, 331-346, and 371-388 • Host: rabbit • Cross Reactivity: (+) human MIZF • Application(s): WB • MIZF protein represses transcription by associating with MBD2 in a histone deacetylase complex.

1 ea



Lane 1: MOLT-4 cell lysate

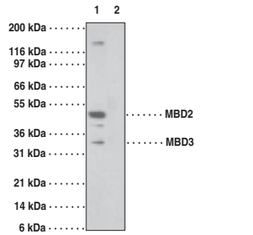




### MBD2/3 Molyclonal Antibody (Clone 106B691) 13773

*Methyl-CpG-Binding Domain 2/3*
Protein G-purified IgG **Stability:** ≥1 year at -20°C
**Summary:** Antigen: human MBD3 amino acids 215-230 • Host: mouse, clone 106B691 • Isotype: $IgG_{1κ}$ • Cross-reactivity: (+) human MBD2/3 • Application(s): WB • MBD2 and MBD3 are members of a family of nuclear proteins related by the presence in each of an MBD. MBD2 is capable of binding specifically to methylated DNA, whereas MBD3 cannot either *in vitro* or *in vivo*.

1 ea



Lane 1: HeLa cell nuclear fraction (Absence of immunizing peptide)
Lane 2: HeLa cell nuclear fraction (Presence of immunizing peptide)

### MeCP2 (human recombinant; methyl binding domain aa 77-166) 11287

*Methyl-CpG Binding Protein 2*
**$M_r$:** 37 kDa **Purity:** ≥95% **Stability:** ≥1 year at -80°C
**Source:** Recombinant N-terminal GST-tagged protein consisting of amino acids 77-166 expressed in *E. coli* • MeCP2 specifically binds to methylated promoters on CpG islands and mediates gene silencing by recruiting corepressor complexes. *In vitro* work suggests high affinity binding of MeCP2 is facilitated by DNA fragments containing A/T bases adjacent to the MeCpG.

25 µg
50 µg
100 µg

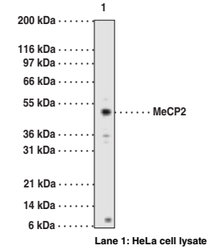


Lane 1: MW Markers
Lane 2: MeCP2 (10 µg)
Lane 3: MeCP2 (5 µg)
Lane 4: MeCP2 (2 µg)

### MeCP2 Polyclonal Antibody 13775

*Methyl-CpG-Binding Protein 2*
Protein G-purified IgG **Stability:** ≥1 year at -20°C
**Summary:** Antigen: human MeCP2 amino acids 11-25 and 181-195 • Host: rabbit • Cross Reactivity: (+) human MeCP2 • Application(s): WB • MeCP2 may function as a mediator of the biological consequences of the methylation signal. It is also reported that this protein functions as a demethylase to activate transcription, as DNA methylation causes gene silencing.

1 ea

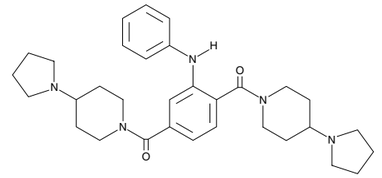


Lane 1: HeLa cell lysate

### UNC1215 13968

*[1415800-43-9]*
**MF:** $C_{32}H_{43}N_5O_2$ **FW:** 529.7 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** A potent, selective chemical probe for the methyl lysine reading function of L3MBTL3 ($K_d$ = 120 nM; $IC_{50}$ = 40 nM) that competitively displaces mono- or dimethyl-lysine containing peptides

1 mg
5 mg
10 mg
50 mg



# Methyltransferases

## Antibodies



## Biochemicals



## Kits



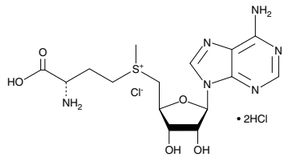
## Proteins



### S-(5′-Adenosyl)-L-methionine chloride (hydrochloride) 13956

*[86867-01-8] AdoMet, SAM*
**MF:** $C_{15}H_{23}ClN_6O_5S$ • 2HCl **FW:** 507.8 **Purity:** ≥95%
A lyophilized powder **Stability:** ≥1 year at -80°C
**Summary:** A ubiquitous methyl donor involved in a wide variety of biological reactions, including those mediated by DNA and protein methyltransferases

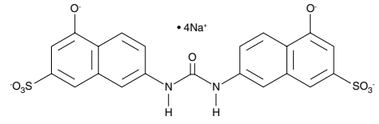
1 mg
2.5 mg
5 mg



### AMI-1 (sodium salt) 13965

*Arginine N-Methyltransferase Inhibitor-1*
**MF:** $C_{21}H_{12}N_2O_9S_2$ • 4Na **FW:** 592.4 **Purity:** ≥99%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** A cell permeable inhibitor of PRMTs; inhibits both yeast Hmt1p and human PRMT1 ($IC_{50}$ = 3.0 and 8.8 µM, respectively); also effectively blocks the activity of PRMTs 3, 4, and 6 but not that of lysine methyltransferases; inhibits HIV-1 reverse transcriptase ($IC_{50}$ = 5.0 µM)

5 mg
25 mg



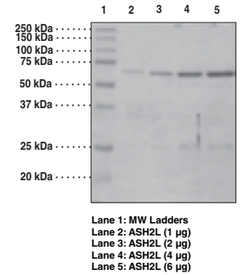




### Ash2L (human recombinant) 10946

*Absent, small, or homeotic discs 2-like, Set1/Ash2 Histone Methyltransferase Complex Subunit Ash2 Isoform A*
**$M_r$:** 60.1 kDa **Purity:** ≥90% **Stability:** ≥6 months at -80°C
**Source:** Recombinant protein consisting of amino acids 96-628 expressed in *E. coli* with a SUMO tag • ASH2L is a component of various multisubunit protein complexes, including the large complex of proteins associated with the SET1 (MLL) family of lysine methyltransferases.

25 µg
50 µg
100 µg

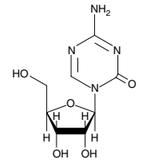


Lane 1: MW Ladders
Lane 2: ASH2L (1 µg)
Lane 3: ASH2L (2 µg)
Lane 4: ASH2L (4 µg)
Lane 5: ASH2L (6 µg)

### 5-Azacytidine 11164

*[320-67-2] Antibiotic U 18496, 5-AzaC, Ladakamycin, Mylosar, NSC 102816, NSC 103-627, WR 183027*
**MF:** $C_8H_{12}N_4O_5$ **FW:** 244.2 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** An inhibitor of DNA methyltransferases that reduces hypermethylation associated with certain diseases, including myelodysplastic syndromes ($IC_{50}$s = 2.4 and 2.6 µM for *in vitro* anti-myeloma activity) and cancer ($IC_{50}$s = ~ 0.4 µM for inhibiting proliferation of various cancer cell lines)

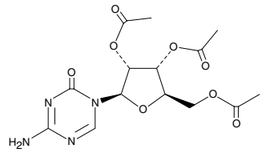
50 mg
100 mg
250 mg



### 2′,3′,5′-triacetyl-5-Azacytidine 13373

*[10302-78-0]*
**MF:** $C_{14}H_{18}N_4O_8$ **FW:** 370.3 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** A prodrug form of 5-azacytidine, an inhibitor of DNA methyltransferases, that may reverse epigenetic changes

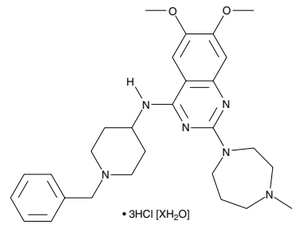
5 mg
10 mg
50 mg
100 mg



### BIX01294 (hydrochloride hydrate) 13124

**MF:** $C_{28}H_{38}N_6O_2$ • 3HCl [$XH_2O$] **FW:** 600.0 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** A selective inhibitor of G9a histone methyltransferase ($IC_{50}$ = 1.7 µM); less effectively inhibits G9a-like protein ($IC_{50}$ = 38 µM) and has no effect on other known histone methyltransferases

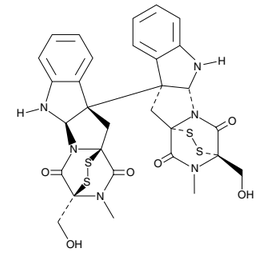
1 mg
5 mg
10 mg
50 mg



### Chaetocin 13156

*[28097-03-2]*
**MF:** $C_{30}H_{28}N_6O_6S_4$ **FW:** 696.8 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** A fungal mycotoxin that inhibits the Lys9-specific histone methyltransferases SU(VAR)3-9 ($IC_{50}$ = 0.8 µM), G9a ($IC_{50}$ = 2.5 µM), and DIM5 ($IC_{50}$ = 3 µM)

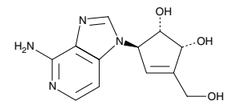
1 mg
5 mg
10 mg



### 3-Deazaneplanocin A 13828

*[102052-95-9] DZNep, NSC 617989*
**MF:** $C_{12}H_{14}N_4O_3$ **FW:** 262.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** An inhibitor of SAH hydrolase; depletes EZH2 levels and inhibits trimethylation of lysine 27 on histone H3 in acute myeloid leukemia cells in a dose-dependent manner (0.2-1 µM); increases expression of the cell-cycle regulators p21, p27, and FBXO32 leading to cell cycle arrest and apoptosis

500 µg
1 mg
5 mg

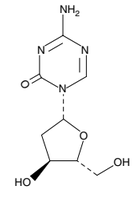


•Also Available: **3-Deazaneplanocin A (hydrochloride)** (11102)

### Decitabine 11166

*[2353-33-5] 5-aza-2′-Deoxycytidine, DAC, Dacogen, NSC 127716*
**MF:** $C_8H_{12}N_4O_4$ **FW:** 228.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** A 2' deoxy analog of 5-azacytidine which is incorporated into DNA and causes hypomethylation by inhibiting DNA methyltransferases in a concentration-dependent manner; useful in conditions characterized by DNA hypermethylation, as is found in myelodysplastic syndromes

5 mg
10 mg
25 mg
50 mg



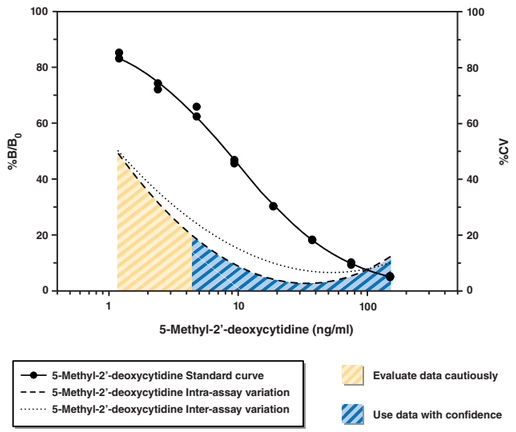
## DNA Methylation EIA Kit 589324

**Stability:** ≥1 year at -20°C
**Sensitivity:** 50% $B/B_0$: 12 ng/ml • 80% $B/B_0$: 3 ng/ml
**Summary:** DNA methylation is an important epigenetic process regulating gene expression. Methylation occurs on carbon 5 of 2'-deoxy-cytidine yielding the modified base 5-methyl-2'-deoxy cytidine. The methylation pattern of cells is tightly regulated during development with the methylation profile being transmitted from parent to daughter cells during cell division. Methylation results in long-term silencing of genes, while unmethylated regions of DNA can be actively transcribed. Global changes in methylation can be quantified by measuring plasma or urinary levels of 5-methyl-2'-deoxy cytidine. These changes in methylation can provide valuable information about cancer status of an individual. For example, patients with leukemia excrete significantly elevated levels of 5-methyl-2'-deoxy cytidine compared to healthy individuals. Global methylation within tissues can be measured in a similar manner, allowing study of tissue-specific changes that occur as a result of differentiation, aging, or carcinogenesis. Cayman's DNA Methylation EIA Kit is a competitive assay that can be used for the quantification of 5-methyl-2'-deoxy cytidine in urine, culture supernatants, plasma, and other sample matrices.
**Specificity:**

| | |
|---|---|
| 5-Methyl-2'-deoxycytidine | 100% |
| 5-Methylcytidine | 20% |
| 2-Deoxycytidine | 0.1% |
| Cytidine | 0.1% |

*For a full specificity profile, please go to www.caymanchem.com*

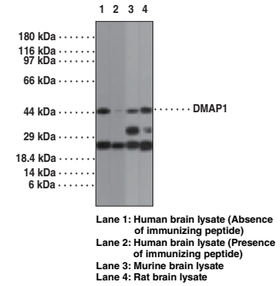
96 solid wells
96 strip wells
480 solid wells
480 strip wells




## DNA Methyltransferase 1-Associated Protein 1 Polyclonal Antibody 13536

*DMAP1*
Protein G-purified IgG **Stability:** ≥1 year at -20°C
**Summary:** Antigen: peptide from human DMAP1 within the region of amino acids 250-300 • Host: rabbit • Cross Reactivity: (+) chimpanzee, bovine, canine, human, mouse, and rat DMAP1 • Application(s): IHC (paraffin-embedded sections) and WB • DMAP1 is involved in the repression or activation of transcription. It is a component of the NuA4 histone acetyltransferase complex and interacts with the transcriptional corepressor tumor susceptibility gene 101 and the pro-apoptotic death-associated protein 6.

1 ea

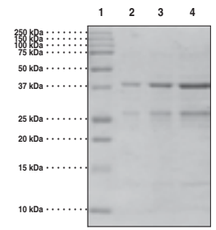


Lane 1: Human brain lysate (Absence of immunizing peptide)
Lane 2: Human brain lysate (Presence of immunizing peptide)
Lane 3: Murine brain lysate
Lane 4: Rat brain lysate

## DNA Methyltransferase 3L (human recombinant) 10770

*DNMT3L, DNMT3-Like Protein*
**$M_r$:** 53.2 kDa **Purity:** ≥95% **Stability:** ≥9 months at -80°C
**Source:** Recombinant N-terminal GST-tagged protein consisting of amino acids 160-387 expressed in *E. coli* • DNMT3L is required to stimulate the DNA methylation activity of DNMT3a and 3b through interactions with the catalytic domain of DNMT3a and 3b.

10 µg
25 µg
50 µg



Lane 1: MW Markers
Lane 2: WDR9 (2 µg)
Lane 3: WDR9 (5 µg)
Lane 4: WDR9 (10 µg)

### DNMT Antibodies

| Item No. | Product Name | Application(s) | Species Specificity |
|---|---|---|---|
| 13479 | DNA Methyltransferase 1 Monoclonal Antibody (Clone 60B1220.1) | WB, IHC (paraffin-embedded sections), ChIP, and IP | (+) Human, mouse, and zebrafish DNMT1 |
| 13481 | DNA Methyltransferase 2 Monoclonal Antibody (Clone 102B1259.2) | WB | (+) Human and mouse DNMT2 |
| 13480 | DNA Methyltransferase 2 Polyclonal Antibody | WB | (+) Human and mouse DNMT2 |
| 13483 | DNA Methyltransferase 3a Monoclonal Antibody - Biotinylated (Clone 64B814.1) | ELISA | (+) Human and mouse DNMT3a |
| 13484 | DNA Methyltransferase 3a Monoclonal Antibody (Clone 64B1446) | WB, IF/ICC, ChIP, and IHC (paraffin) | (+) Human and mouse DNMT3a |
| 13482 | DNA Methyltransferase 3a Monoclonal Antibody (Clone 64B814.1) | WB, IF, and ICC | (+) Human and mouse DNMT3a |
| 13485 | DNA Methyltransferase 3b Monoclonal Antibody (Clone 52A1018) | WB, IP, IF, ICC, ChIP, and IHC (paraffin) | (+) Human and mouse DNMT3b |

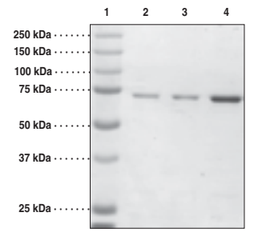




## Dot1L (human recombinant) 10354

*Disruptor of Telomeric Signaling 1-Like, Dot1-like*
**$M_r$:** 74.1 kDa **Purity:** ≥95% **Stability:** ≥6 months at -80°C
**Source:** Active recombinant N-terminal GST-tagged protein consisting of amino acids 2-416 expressed in *E. coli* • Dot1L is a non-SET domain containing methyltransferase that is the only enzyme known to methylate histone 3 at lysine 79, where it catalyzes mono-, di-, and trimethylation. Proper Dot1L function is necessary for transcriptional activation of many genes, DNA damage repair, and cell cycle regulation.

25 µg
50 µg
100 µg

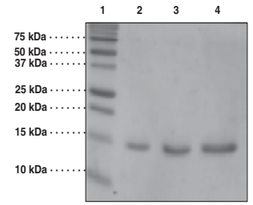


Lane 1: MW Markers
Lane 2: Dot1L (1 µg)
Lane 3: Dot1L (2 µg)
Lane 4: Dot1L (4 µg)

## DPY-30 (human recombinant) 11178

*DPY-30-Like protein, hDPY-30, SAF19*
**$M_r$:** 11.2 kDa **Purity:** ≥95% **Stability:** ≥6 months at -80°C
**Source:** Recombinant protein consisting of amino acids 2-99 expressed in *E. coli* • DPY-30 is a component of the MLL1 methylation complex, which interacts directly with Ash2L.

25 µg
50 µg
100 µg



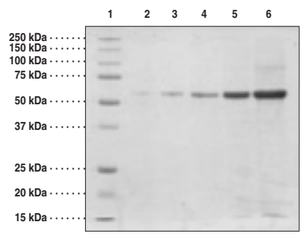
Lane 1: MW Markers
Lane 2: DPY-30 (1 µg)
Lane 2: DPY-30 (2 µg)
Lane 2: DPY-30 (4 µg)

*NOTE: SUMO Affinity tag used under license from LifeSensors, Inc.*

## EED (human recombinant) 10628

*Embryonic Ectoderm Development*
**$M_r$:** 53.5 kDa **Purity:** ≥95% **Stability:** ≥9 months at -80°C
**Source:** Recombinant N-terminal His-tagged protein consisting of amino acids 1-441 expressed in Sf21 cells • EED is a WD40 repeat-containing protein that forms part of the PRC2. The EED subunit does not contain methyltransferase activity. However, transcriptional repression by PRC2-mediated trimethylation of lysine 27 on Histone H3 has been shown to be dependent on EED binding to repressive histone marks.

25 µg
50 µg
100 µg

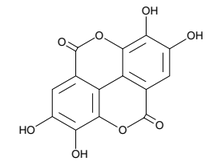


Lane 1: MW Standards
Lane 2: Pure EED (0.5 µg)
Lane 3: Pure EED (1 µg
Lane 4: Pure EED (2 µg)
Lane 5: Pure EED (5 µg)
Lane 6: Pure EED (10 µg)

## Ellagic Acid 10569

*[476-66-4] Gallogen, Lagistase, TBBD*
**MF:** $C_{14}H_6O_8$ **FW:** 302.2 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** A polyphenolic antioxidant that is abundant in many fruits, vegetables, plant bark, and peels; has anti-carcinogenic, anti-mutagenic, anti-inflammatory, and organ-preserving properties; blocks methylation of H3R17 by CARM1 without significantly altering histone acetylase or DNA methyltransferase activity

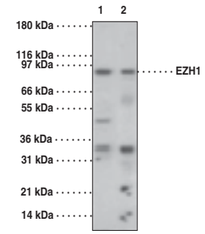
100 mg
500 mg
1 g




## EZH1 Polyclonal Antibody 13487

Protein G-purified IgG **Stability:** ≥1 year at -20°C
**Summary:** Antigen: peptides of human EZH1 • Host: rabbit • Cross Reactivity: (+) human and mouse EZH1 • Application(s): WB • EZH1 is a human homolog of the *Drosophila* gene-enhancer of zeste, a member of the polycomb group of transcriptional repressors. It has a potential role in human development as a transcriptional regulator and a component of protein complexes that stably maintain heterochromatin.

1 ea

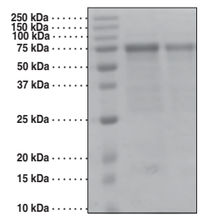


Lane 1: Mouse spleen lysate
Lane 2: Human spleen lysate

## G9a (human recombinant) 10353

*EHMT2, Euchromatic Histone-Lysine N-Methyltransferase 2, KMT1C*
**$M_r$:** 75.4 kDa **Purity:** ≥70% **Stability:** ≥6 months at -80°C
**Source:** Active recombinant N-terminal GST-tagged protein consisting of amino acids 785-1,210 expressed in *E. coli* • G9a is a SET domain-containing methyltransferase that specficially mono- and di-methylates Histone H3K9 at lysine 9.

25 µg
50 µg
100 µg



Lane 1: MW Markers
Lane 2: G9a (5 µg)
Lane 3: G9a (2.5 µg)

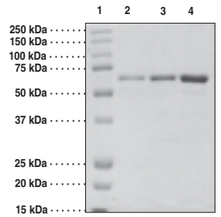
## G9a-like protein (human recombinant) 10755

*EHMT1, Euchromatic Histone-Lysine N-Methyltransferase 1, Eu HMTase 1, GLP, KMT1D*

**M.:** 60.3 kDa **Purity:** ≥95% **Stability:** ≥6 months at -80°C

**Source:** Active recombinant N-terminal GST-tagged protein consisting of amino acids 1,004-1,298 expressed in *E. coli* • GLP is a SET domain-containing methyltransferase that specifically mono- and di-methylates H3K9.

25 µg
50 µg
100 µg




Lane 1: MW Markers
Lane 2: GLP (1 µg)
Lane 3: GLP (2 µg)
Lane 4: GLP (5 µg)

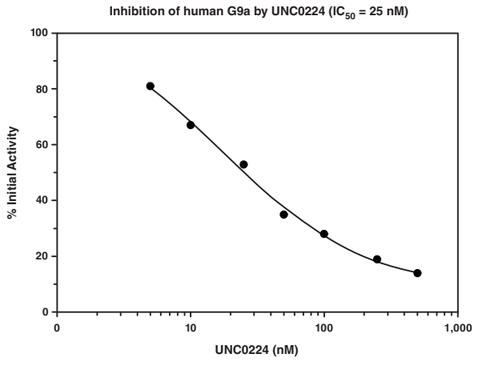
## G9a Methyltransferase Inhibitor Screening Assay Kit 700500

*EHMT2*

**Stability:** ≥6 months at -80°C

**Summary:** G9a is a SET domain-containing mammalian histone methyltransferase that can mono- or dimethylate lysine 9 and lysine 27 on histone H3. G9a is overexpressed in various cancers and is a potential inhibitory target for cancer treatment. In Cayman's G9a Methyltransferase Inhibitor Screening Assay, the transfer of the methyl group from SAM to the acceptor peptide by G9a generates SAH, which is rapidly converted to urate and $H_2O_2$ using an enzyme mixture provided in the kit. A subsequent reaction between $H_2O_2$ and ADHP produces the highly fluorescent compound resorufin.

96 wells



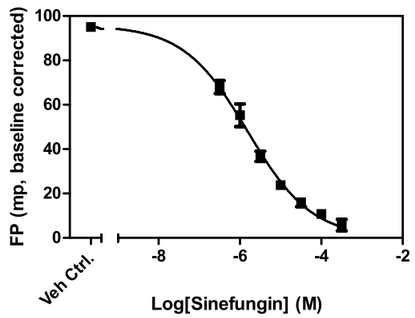

## GLP SAM-Screener™ Assay Kit 600570

*G9a-like protein*

**Stability:** ≥6 months at -80°C **Z' Factor:** 0.56

**Summary:** G9a-like protein is a SET domain-containing methyltransferase that specifically mono- and di-methylates H3K9. GLP and G9a function as major euchromatic H3K9me1 and H3K9me2 histone methyltransferases and also have been found to methylate several nonhistone substrates, including p53(K372). This fluorescence polarization assay is based upon a proprietary small molecule fluorescent probe that binds to the SAM binding pocket in GLP. Binding of the small molecule probe to GLP induces an increase in fluorescence polarization. Binding of the probe can be competed with the endogenous cofactor SAM or by the inhibitor sinefungin, but is unaffected by the histone H3 peptide substrate. The GLP SAM-Screener Assay is robust and exhibits a greater than 80 mP shift over a range of 0-250 nM GLP. The assay is suitable for high-throughput screening in the provided 384-well plate or can be scaled to higher density plate formats (*e.g.*, 1,536-well) if desired.

384 wells
1,920 wells



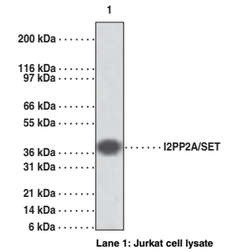

## I2PP2A/SET Polyclonal Antibody 13782

*Inhibitor of granzyme A-activated DNase, PHAPII, Phosphatase 2A Inhibitor, Template-Activating Factor I*

Protein G-purified IgG **Stability:** ≥1 year at -20°C

**Summary:** Antigen: synthetic peptides from human I2PP2A/SET amino acids 79-94 and 148-164 • Host: rabbit • Cross Reactivity: (+) human I2PP2A/SET • Application(s): WB • I2PP2A/SET is a multitasking protein, involved in apoptosis, transcription, nucleosome assembly, and histone binding.

1 ea




Lane 1: Jurkat cell lysate

## Methylated Lysine Polyclonal Antibody 13727

Affinity-purified IgG **Stability:** ≥1 year at -20°C

**Summary:** Antigen: methylated KLH • Host: rabbit • Cross Reactivity: (+) mono- and di-methylated lysine residues; (-) acetylated lysine • Application(s): ELISA, IHC, IP, and WB • Lysine can be methylated once, twice, or three times by lysine methyltransferases. The transfer of methyl groups from SAM to histones is catalyzed by histone methyltransferases.

400 µl



## Methylated Lysine Polyclonal Antibody-biotin 13728

Affinity-purified IgG **Stability:** ≥1 year at -20°C

**Summary:** Antigen: methylated KLH • Host: rabbit • Cross Reactivity: (+) methylated lysine residues • Application(s): ELISA, IP, and WB • Lysine can be methylated once, twice, or three times by lysine methyltransferases. The transfer of methyl groups from SAM to histones is catalyzed by histone methyltransferases.

400 µl

## Methylated Lysine Polyclonal Antibody HRP Conjugate 13729

Affinity-purified IgG **Stability:** ≥1 year at -20°C

**Summary:** Antigen: methylated KLH • Host: rabbit • Cross Reactivity: (+) methylated lysine residues • Application(s): ELISA and WB • Lysine can be methylated once, twice, or three times by lysine methyltransferases. The transfer of methyl groups from SAM to histones is catalyzed by histone methyltransferases.

400 µl

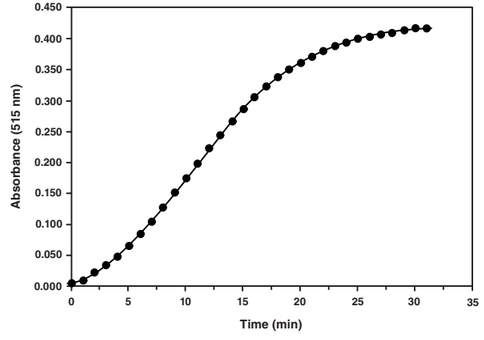
## Methyltransferase Colorimetric Assay Kit 700140

*MT*

**Stability:** ≥6 months at -80°C

**Summary:** Cayman's Methyltransferase Colorimetric Assay Kit is a continuous enzyme-coupled assay that can continuously monitor SAM-dependent methyltransferases. The removal of the methyl group from SAM generates AdoHcy, which is rapidly converted to urate and $H_2O_2$ by an enzyme mixture provided in the kit. The rate of production of $H_2O_2$ is measured with the colorimetric reagent, 3,5-dichloro-2-hydroxybenzenesulfonic acid, by an increase in absorbance at 500-520 nm. The assay is supplied with AdoHcy as a positive control. The assay can be used with any purified SAM-dependent methyltransferase.

96 wells



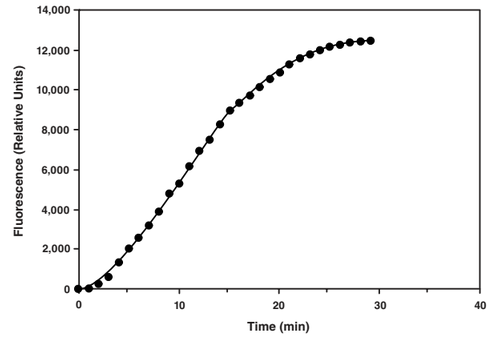

## Methyltransferase Fluorometric Assay Kit 700150

*MT*

**Stability:** ≥6 months at -80°C

**Summary:** Cayman's MT Fluorometric Assay is a continuous enzyme-coupled assay that can continuously monitor SAM-dependent MTs. The removal of the methyl group from SAM generates AdoHcy, which is rapidly converted to urate and $H_2O_2$ by an enzyme mixture provided in the kit. The reaction between $H_2O_2$ and ADHP produces the highly fluorescent compound resorufin, which is analyzed with an excitation wavelength of 530-540 nm and an emission wavelength of 585-595 nm. The assay is supplied with AdoHcy as a positive control. The assay can be used with any purified SAM-dependent MT.

96 wells



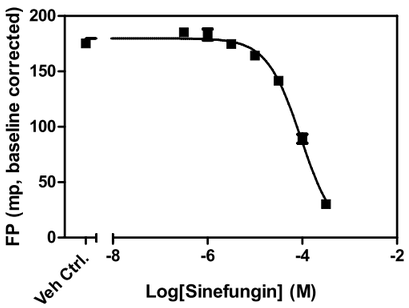

## MLL1 SAM-Screener™ Assay Kit 600580

*Mixed-Lineage Leukemia-1*

**Stability:** ≥6 months at -80°C **Z' Factor:** 0.71

**Summary:** MLL1 is a member of the trithorax group (trxG)/Set1-like family of gene activators that contains histone methyltransferase activity specific for lysine 4 of histone H3. This methylation plays an important role in gene activation at various developmentally regulated loci, such as the Hox gene loci. This fluorescence polarization assay is based upon a proprietary small molecule fluorescent probe that binds to the SAM binding pocket in MLL1. Binding of the small molecule probe to MLL1 induces an increase in fluorescence polarization. Binding of the probe can be competed with the endogenous cofactor SAM or by the inhibitor sinefungin, but is unaffected by the histone H3 peptide substrate. The MLL1 SAM-Screener Assay is robust and exhibits a greater than 100 mP shift over a range of 0-500 nM MLL1. The assay is suitable for high-throughput screening in the provided 384-well plate or can be scaled to higher density plate formats (*e.g.*, 1,536-well) if desired.

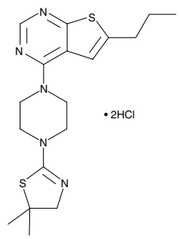
384 wells
1,920 wells



## MI-2 (hydrochloride) 11620

**MF:** $C_{18}H_{25}N_5S_2$ • 2HCl **FW:** 448.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** Potently binds menin, blocks the menin-MLL fusion protein interaction ($IC_{50}$ = 0.45 µM), and induces apoptosis in cells expressing MLL fusion proteins

1 mg
5 mg
10 mg
25 mg

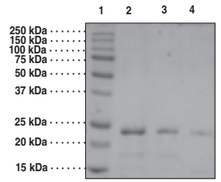



• Also Available: **MI-nc (hydrochloride)** (11621)

## MLL1 (human recombinant) 10658

*ALL1, HRX, KMT2A, Lysine Methyltransferase 2A, Mixed Lineage Leukemia-1*
**$M_r$:** 24.1 kDa **Purity:** ≥95% **Stability:** ≥6 months at -80°C
**Source:** Recombinant protein consisting of amino acids 3,762-3,969 expressed in *E. coli* • MLL1 plays a major role in epigenetic regulation through methylation of H3K4 to activate gene transcription.

50 µg
100 µg
250 µg




**Lane 1: MW Markers**
**Lane 2: MLL1 (4 µg)**
**Lane 3: MLL1 (2 µg)**
**Lane 4: MLL1 (1 µg)**

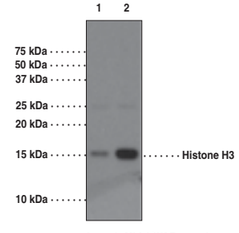
*NOTE: SUMO Affinity tag used under license from LifeSensors, Inc.*

## MLL1/WAR complex (human recombinant) 10756

*Mixed-Lineage Leukemia-1, MLL Core Complex*
**$M_r$:** 180 kDa **Purity:** ≥90% **Stability:** ≥6 months at -80°C
**Source:** Active recombinant proteins expressed in *E. coli*. MLL1, WDR5, Ash2L, and RbBP5 are expressed with N-terminal His-SUMOpro affinity tags. The His-SUMO affinity tags were removed using recombinant SUMO Protease 1 • The MLL complex methylates H3K4 to upregulate transcription. MLL1 is the catalytic subunit which exhibits a low basal methyltransferase activity. Addition of WDR5, Ash2L, and RbBP5 (WAR) enhances Histone H3K4 methylation 300-fold.

100 µg
250 µg
500 µg

**Autoradiograph of Core Histone (Cayman Item No. 11010) separated on SDS-PAGE following reaction with [$^3$H]-SAM and the MLL1/WAR complex.**




**Lane 1: MLL1/WAR complex (1 µM each of MLL1, Ash2L, RbBP5, WDR5)**
**Lane 2: MLL1/WAR complex (3 µM each of MLL1, Ash2L, RbBP5, WDR5)**

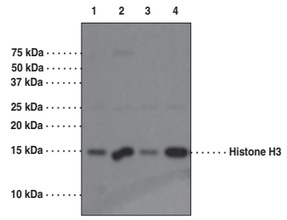
*NOTE: SUMO Affinity tag used under license from LifeSensors, Inc.*

## MLL1/WARD complex (human recombinant) 10945

*KMT2A, Mixed-Lineage Leukemia-1, MLL Core Complex*
**$M_r$:** ~200.1 kDa **Purity:** ≥90% **Stability:** ≥6 months at -80°C
**Source:** Active recombinant proteins expressed in *E. coli*. MLL1, WDR5, Ash2L, RbBP5, and DPY-30 are expressed with N-terminal His-SUMOpro affinity tags. The His-SUMO affinity tags were removed using recombinant SUMO Protease 1 • The MLL complex methylates H3K4 to upregulate transcription. MLL1 is the catalytic subunit and contains the core components WDR5, Ash2L, and RbBP5 (MLL/WAR complex). MLL1 alone exhibits a low basal methyltransferase activity, but is enhanced 300-fold by the addition of the WAR components. A further 2-fold activation has been reported with the addition of DPY-30 (MLL/WARD complex).

100 µg
250 µg
500 µg

**Autoradiograph of Core Histone (Cayman Item No. 11010) separated on SDS-PAGE following reaction with [$^3$H]-SAM and the MLL1/WARD complex or MLL1/WAR complex.**



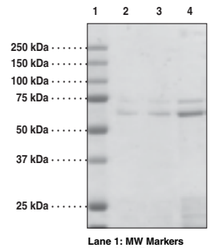

**Lane 1: MLL1/WARD complex (1 µM each of MLL1, Ash2L, RbBP5, WDR5, DPY-30)**
**Lane 2: MLL1/WARD complex (3 µM each of MLL1, Ash2L, RbBP5, WDR5, DPY-30)**
**Lane 3: MLL1/WAR complex (1 µM each of MLL1, Ash2L, RbBP5, WDR5)**
**Lane 4: MLL1/WAR complex (3 µM each of MLL1, Ash2L, RbBP5, WDR5)**

*NOTE: SUMO Affinity tag used under license from LifeSensors, Inc.*

## NSD1 (human recombinant) 10757

*AR267, KMT3B, Nuclear Receptor SET domain-containing protein 1, WHSC1*
**$M_r$:** 60.2 kDa **Purity:** ≥60% **Stability:** ≥1 year at -80°C
**Source:** Active recombinant N-terminal GST-tagged protein consisting of amino acids 1,700-1,986 expressed in *E. coli* • NSD1 methylates H3K36 and H4K20 and is important for maintaining chromatin integrity. It contains a catalytic lysine methyltransferase SET domain and four zinc-binding PHD fingers.

25 µg
50 µg
100 µg




**Lane 1: MW Markers**
**Lane 2: NSD1 (1 µg)**
**Lane 3: NSD1 (2 µg)**
**Lane 4: NSD1 (5 µg)**

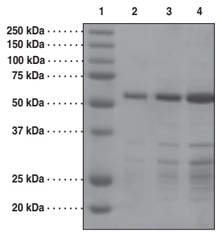




## NSD2 (human recombinant) 10758

*Histone-lysine N-methyltransferase NSD2 isoform 1, KIAA1090, MMSET, Nuclear Receptor SET domain-containing protein 2, Protein trithorax-5, TRX5, WHSC1*
**$M_r$:** 61.2 kDa **Purity:** ≥90% **Stability:** ≥1 year at -80°C
**Source:** Active recombinant N-terminal GST-tagged protein consisting of amino acids 941-1,240 expressed in *E. coli* • NSD2 has been implicated in multiple myeloma, an incurable malignancy in mature plasma cells, being involved in recurrent t(4;14) translocations with the immunoglobulin promotor/enhancer. NSD2 is responsible for the post-translational modification of histones H3 and H4. The methylation target of NSD2 is dependent on the nature of the substrate.

25 µg
50 µg
100 µg

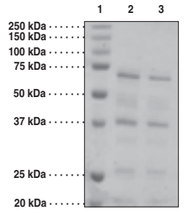



**Lane 1: MW Markers**
**Lane 2: NSD2 (1 µg)**
**Lane 3: NSD2 (5 µg)**
**Lane 4: NSD2 (10 µg)**

## PRDM9 (human recombinant) 11209

*Meisetz, MSBP3, PFM6, PR Domain-containing Protein 9, ZNF899*
**$M_r$:** 60.5 kDa **Purity:** ≥65% **Stability:** ≥6 months at -80°C
**Source:** Active recombinant N-terminal His-tagged protein consisting of amino acids 2-511 expressed in *E. coli* • PRDM9 is a histone methyltransferase that binds specifically to recombination hotspots catalyzing trimethylation of H3K4 in nucleosomes near its binding site, thus initiating genetic recombination by recruiting recombination initiation machinery.

10 µg
25 µg
50 µg

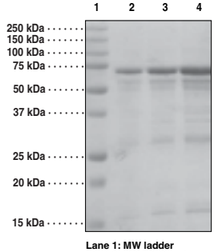



**Lane 1: MW Markers**
**Lane 2: PRDM9 (4 µg)**
**Lane 3: PRDM9 (2 µg)**

## PRMT1 (human recombinant) 10350

*Protein Arginine Methyltransferase 1*
**$M_r$:** 69.2 kDa **Purity:** ≥80% **Stability:** ≥6 months at -80°C
**Source:** Active recombinant N-terminal GST-tagged protein consisting of amino acids 2-371 expressed in *E. coli* • PRMT1 is a class I arginine methyltransferase that methylates arginine residues at a number of glycine and arginine rich regions including histone H4 at arginine 3.

25 µg
50 µg
100 µg

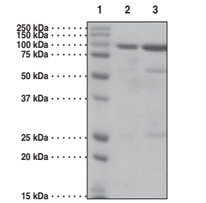



**Lane 1: MW ladder**
**Lane 2: PRMT1 (1 µg)**
**Lane 3: PRMT1 (2 µg)**
**Lane 4: PRMT1 (4 µg)**

## PRMT3 (human recombinant) 11642

*Heterogeneous Nuclear Ribonucleoprotein Methyltransferase-like Protein 3, Protein Arginine methyltransferase 3*
**$M_r$:** 86.6 kDa **Purity:** ≥90% **Stability:** ≥6 months at -80°C
**Source:** Active recombinant N-terminal GST-tagged protein consisting of amino acids 2-531 expressed in *E. coli* • PRMT3 is a type-1 PRMT, catalyzing the formation of MMA and ADMA.

25 µg
50 µg
100 µg

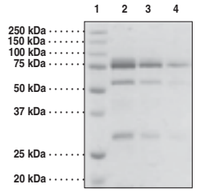



**Lane 1: MW Markers**
**Lane 2: PRMT3 (2.5 µg)**
**Lane 3: PRMT3 (5 µg)**

## PRMT4 (human recombinant) 10750

*CARM1, Protein Arginine Methyltransferase 4*
**$M_r$:** 92.6 kDa **Purity:** ≥70% **Stability:** ≥1 year at -80°C
**Source:** Active recombinant N-terminal GST-tagged protein consisting of amino acids 2-608 expressed in *E. coli* • PRMT4, also known as CARM1, is a type-1 PRMT, catalyzing MMA and ADMA on histone H3, Arg-17, and Arg-26.

25 µg
50 µg
100 µg

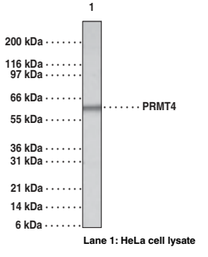



**Lane 1: MW Markers**
**Lane 2: PRMT4 (5 µg)**
**Lane 2: PRMT4 (2.5 µg)**
**Lane 2: PRMT4 (1.25 µg)**

## PRMT4 Polyclonal Antibody 13552

*CARM1*
Protein G-purified IgG **Stability:** ≥1 year at -20°C
**Summary:** Antigen: human PRMT4 amino acid sequences 45-69 and 595-608 • Host: rabbit • Cross Reactivity: (+) human PRMT4 • Application(s): WB • PRMT4, also known as CARM1, belongs to a family of proteins that catalyzes the methylation of arginine residues.

1 ea

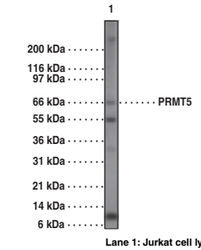



**Lane 1: HeLa cell lysate**

## PRMT5 Polyclonal Antibody 13559

*JBP1, Skb1HS*
Protein G-purified IgG **Stability:** ≥1 year at -20°C
**Summary:** Antigen: human PRMT5 • Host: rabbit • Cross Reactivity:(+) human PRMT5 • Application(s): WB • PRMT5, also known as JBP1 and human homolog of Skb1 of fission yeast (Skb1HS), can catalyze the formation of MMA and symmetric dimethylarginine in a variety of proteins. Recombinant PRMT5 can mono- and dimethylate histone 2A and myelin basic protein.

1 ea

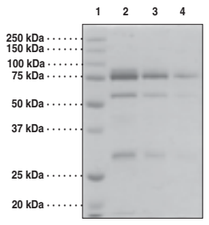


Lane 1: Jurkat cell lysate

## PRMT6 (human recombinant) 10752

*Histone Arginine N-methyltransferase PRMT6, HRMT1L6, Protein Arginine Methyltransferase 6*
**$M_r$:** 68.7 kDa **Purity:** ≥80% **Stability:** ≥1 year at -80°C
**Source:** Active recombinant N-terminal GST-tagged protein consisting of amino acids 2-375 expressed in *E. coli* • PRMT6 is a nuclear type-1 PRMT, catalyzing the formation of MMA and ADMA on both histone and non-histone targets.

25 µg
50 µg
100 µg

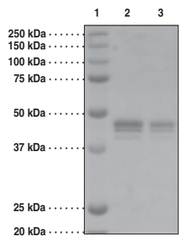


Lane 1: MW Markers
Lane 2: PRMT6 (5 µg)
Lane 3: PRMT6 (2.5 µg)
Lane 4: PRMT6 (1.25 µg)

## PRMT6 (human recombinant; baculovirus expressed) 13866

*Histone Arginine N-methyltransferase PRMT6, HRMT1L6, Protein Arginine Methyltransferase 6*
**$M_r$:** 43.7 kDa **Purity:** ≥60% **Stability:** ≥1 year at -80°C
**Source:** Active recombinant N-terminal His-tagged protein consisting of amino acids 2-375 expressed in *Sf*21 cells • PRMT6 is a nuclear type-1 PRMT, catalyzing the formation of MMA and ADMA on both histone and non-histone targets. Non-histone targets of PRMT6 include the nuclear high-mobility group (HMG) protein HMGA1a, a protein important in several processes relating to the maintainence of DNA integrity.

25 µg
50 µg
100 µg

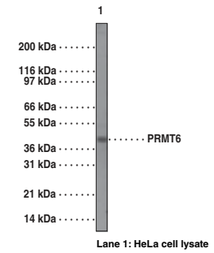


Lane 1: MW Markers
Lane 2: PRMT6 (4 µg)
Lane 3: PRMT6 (2 µg)

## PRMT6 Polyclonal Antibody 13558

Protein G-purified IgG **Stability:** ≥1 year at -20°C
**Summary:** Antigen: human PRMT6 amino acids 23-43 • Host: rabbit • Cross Reactivity:(+) human and mouse PRMT6 • Application(s): WB • PRMT6 is a protein with an approximate molecular weight of 42 kDa consisting of a catalytic core sequence common to other PRMT enzymes. PRMT6 demonstrates type 1 PRMT activity, capable of forming both MMA and ADMA derivatives on recombinant glycine- and arginine-rich substrates.

1 ea

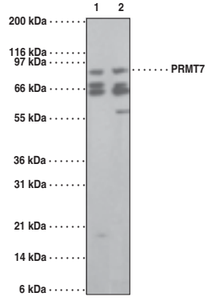


Lane 1: HeLa cell lysate

## PRMT7 Polyclonal Antibody 13551

Protein G-purified IgG **Stability:** ≥1 year at -20°C
**Summary:** Antigen: human PRMT7 amino acids 346-360 • Host: rabbit • Cross Reactivity:(+) human and mouse PRMT7 • Application(s): WB • PRMT7 can catalyze the formation of MMA in peptides.

1 ea

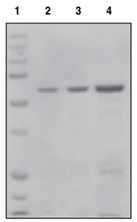


Lane 1: HeLa cell lysate
Lane 2: NIH 3T3 cell lysate

## PRMT8 (human recombinant) 11644

*HRMT1L, Protein Arginine Methyltransferase 8*
**$M_r$:** 65.7 kDa **Purity:** ≥90% **Stability:** ≥9 months at -80°C
**Source:** Active recombinant N-terminal GST-tagged protein consisting of amino acids 61-394 expressed in *E. coli* • PRMT8 is a type I methyltransferase shown to methylate the glycine-arginine rich region in fibrillarin. Its expression is limited to the brain.

25 µg
50 µg
100 µg



Lane 1: MW Markers
Lane 2: PRMT8 (1 µg)
Lane 3: PRMT8 (2 µg)
Lane 4: PRMT8 (5 µg)

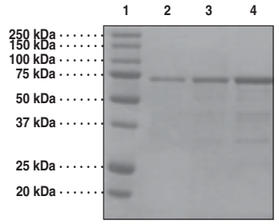




## RbBP5 (human recombinant) 10947

*RBQ-3, Retinoblastoma-binding Protein 5, SWD1/Set1c WD40 repeat protein homolog*
**$M_r$:** 72.9 kDa **Purity:** ≥90% **Stability:** ≥6 months at -80°C
**Source:** Recombinant protein consisting of amino acids 2-538 expressed in *E. coli* • RbBP5 is a ubiquitously expressed nuclear protein that contains WD40 repeat-like domains. RbBP5 binds directly to tumor suppressor retinoblastoma protein and regulates cell proliferation. RbBP5 is also an important component of the multi-subunit SET1 lysine methyltransferase protein complex, which includes MLL1.

25 µg
50 µg
100 µg

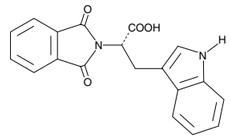


Lane 1: MW Markers
Lane 2: RbBP5 (1 µg)

## RG-108 13302

*[48208-26-0] N-Phthalyl-L-Tryptophan*
**MF:** $C_{19}H_{14}N_2O_4$ **FW:** 334.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** A non-nucleoside DNA methyltransferase inhibitor ($IC_{50}$ = 115 nM *in vitro*) that significantly reduces the methylation of genomic DNA in cells at 10 µM without detectable toxicity

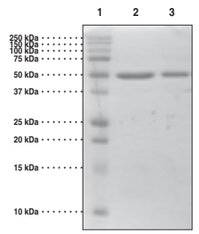
5 mg
10 mg
50 mg
100 mg




## RIZ1 (human recombinant) 10765

*KMT8, PRDM2, PR Domain Zinc Finger Protein 2, Retinoblastoma Protein-interacting Zinc Finger Protein*
**$M_r$:** 49.5 kDa **Purity:** ≥95% **Stability:** ≥6 months at -80°C
**Source:** Recombinant N-terminal GST-tagged protein consisting of amino acids 2-200 expressed in *E. coli* • RIZ1 is a SAM-dependent histone methyltransferase that specifically methylates H3K9. RIZ1 is a tumor suppressor that can arrest the cell cycle and induce apoptosis.

50 µg
100 µg
250 µg

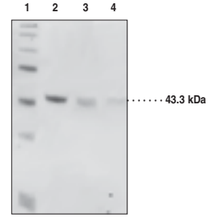


Lane 1: MW Markers
Lane 2: RIZ1 (5 µg)
Lane 3: RIZ1 (2.5 µg)

## SET7/9 (human recombinant) 10320

*KMT7, SETD7/9, SET Domain-Containing Protein 7/9*
**$M_r$:** 43.3 kDa **Purity:** ≥95% **Stability:** ≥6 months at -80°C
**Source:** Active recombinant N-terminal His-tagged SET7/9 amino acids 1-366 expressed in *E. coli* • SET7/9 is exclusively a mono-methylase that methylates histone H3, tumor suppressor p53, and transcription factor TAF10. SET7/9 methylates p53 in response to DNA damage thereby activating p53 for subsequent acetylation.

25 µg
50 µg
100 µg

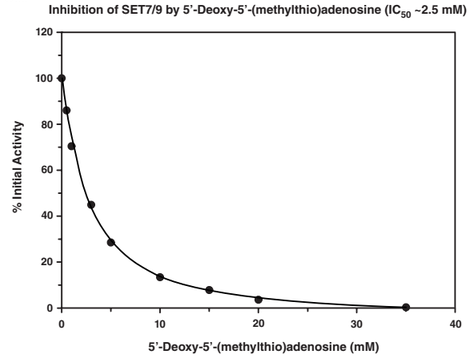


Lane 1: MW Markers
Lane 2: SET7/9 (4 µg)
Lane 3: SET7/9 (1 µg)
Lane 4: SET7/9 (0.5 µg)

## SET7/9 Methyltransferase Inhibitor Screening Assay Kit 700270

**Stability:** ≥6 months at -80°C
**Summary:** SET7/9 is an MT that acts on various substrates including H3K4, p53, and the transcription factor TAF 10. In Cayman's SET7/9 MT Inhibitor Screening Assay the transfer of the methyl group from SAM by SET7/9 to the acceptor peptide (TAF 10) generates SAH, which is rapidly converted to urate and $H_2O_2$ using an enzyme mixture provided in the kit. A subsequent reaction between $H_2O_2$ and ADHP produces the highly fluorescent compound resorufin.

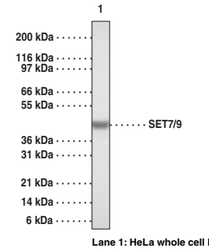
96 wells




## SET7/9 Polyclonal Antibody 13731

Protein G-purified IgG **Stability:** ≥1 year at -20°C
**Summary:** Antigen: human SET7/9 amino acids 131-145 and 336-352 • Host: rabbit • Cross Reactivity: (+) mouse and human SET7/9 • Application(s): WB • SET7/9 is a histone specific HMTase that methylates histone H3K4.

1 ea



Lane 1: HeLa whole cell lysate

# Histone Methylation and the Language of Epigenetics

by [Thomas G. Brock, Ph.D.]

The basic processes of chromatin modification which influence gene expression are familiar to many of us: the addition and removal of acetyl and methyl marks, phosphorylation, ubiquitination, and so on. However, the exciting part, the complexity of how the marks are used, is just emerging. Some of the new terminology related to this, such as 'epigenetic editing', 'reading', and 'writing', begins to hint that chromatin modification is much like a language.[1,2] This means that, perhaps, we have just learned some of the basic letters or words, with the more challenging issues of grammar, literal meaning, innuendo, and misleading information still to be contemplated.[3] Consider the discovery of the four 'letters' of DNA, which was found to encode messages that were divided into segments, complete with phrases for starting and stopping and much, much more. We are still learning how to decipher the more complex information generated by these four letters. By analogy, a methylated lysine mark is one of the letters of epigenetic signaling. This article considers histone methylation and suggests directions for understanding its meaning.

## Lysine Methyltransferases

Braille, the writing system developed for the visually impaired, uses a simple raised mark as its basic unit. Importantly, it is the organization of raised marks which creates a letter and, of course, you need a series of these to produce words and sentences. In the same way, a methyl mark is a basic unit of epigenetic 'reading'. This mark can be attached to lysine (K) or arginine (R) on proteins as well as to cytosine on DNA. Up to three methyl groups can be added to K while R can be monomethylated as well as symmetrically or asymmetrically dimethylated. Should each of these be viewed, like Braille letters with different arrangements of raised dots, as being distinct letters of the epigenetic language? Certainly monomethylation at the three types of targets (K, R, cytosine) produces three distinct structures that are written, erased, and, most importantly, read by binding domains that are unique to each.

| Common Name | KMT Name | Mark |
|---|---|---|
| SUV39H1 | KMT1A | H3K9me3 |
| SUV39H2 | KMT1B | H3K9me3 |
| EHMT2, G9A | KMT1C | H3K9me1,2, H3K27me, H3K56me1 |
| EHMT1, GLP | KMT1D | H3K9me1,2, H3K27me |
| SETDB1 | KMT1E | H3K9me3 |
| SETCB2 | KMT1F | H3K9me3 |
| MLL | KMT2A | H3K4me |
| MLL4 | KMT2B | H3K4me |
| MLL3 | KMT2C | H3K4me |
| MLL2 | KMT2D | H3K4me |
| MLL5 | KMT2E | H3K4me1,2 |
| SETD1A, SET1A | KMT2F | H3K4me |
| SETD1B, SET1B | KMT2G | H3K4me |
| ASH1L | KMT2H | H3K4me, H3K36me |
| SETD2, SET2 | KMT3A | H3K36me |
| NSD1 | KMT3B | H3K36me, H4K20me |
| SMYD2 | KMT3C | H3K4me, H3K36me2 |
| DOT1L | KMT4 | H3K79me |
| SET8, SETD8 | KMT5A | H4K20me1 |
| SUV420H1 | KMT5B | H4K20me3 |
| SUV420H2 | KMT5C | H4K20me3 |
| EZH2 | KMT6 | H3K9me, H3K27me1,2,3 |
| SET7/9, SETD7 | KMT7 | H3K4me |

**Table 1. Human lysine methyltransferases**

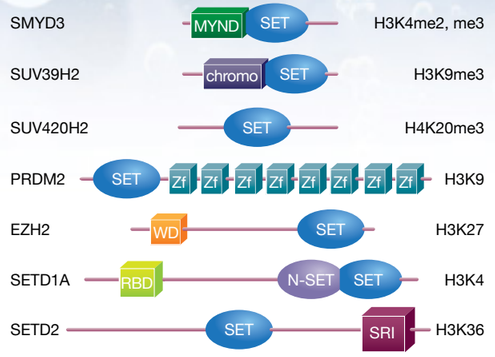



**Figure 1. Structural organization of representative SET domain-containing proteins**

Focusing on lysine methyltransferases (KMTs), a list of those that have been assigned KMT names (Table 1) provides more information. There clearly is duplication of KMTs, with two similar enzymes making the same mark. This may indicate that the function of each pair is important enough to require a backup should one of the pair fail. Alternatively, the pair afford distinct regulatory pathways or tissue specific expression. In addition, methylation at H3K4 can be performed by a wide number of KMTs. Possibly, this mark is essential to chromatin housekeeping and plays only a general role in the epigenetic language. Finally, some enzymes specialize in monomethylating a particular residue (*e.g.*, SET8 at H4K20) while others specifically di- or trimethylate (*e.g.*, SUV420H1 and 2 at H4K20). This suggests that, at least in some cases, the accumulation of methyl groups at a given site is regulated, indicating that being trimethylated can have a different meaning from being monomethylated.

## SET Domain Proteins

Additional insights may be derived from the methyl writers. To make the mark, many KMTs contain a SET domain, named after regions shared by three *Drosophila* proteins recognized as being involved in epigenetic processes: Su(var)3-9, Enhancer of zeste, and Trithorax. The SET domain includes conserved N- and C- terminal regions (SET-N, SET-C) and an intervening insert region (SET-I). Flanking pre- and post-SET regions are typically also required for full KMT activity.

Some KMTs have multiple functions. For example, the SMYD proteins are short KMTs that contain SET and MYND-type zinc finger domains (Figure 1). Like other zinc finger domains, MYND domains are involved in protein-protein interactions, commonly binding a co-repressor protein, like NCoR or SMRT. SMYD1 acts as a transcriptional repressor, is essential for cardiomyocyte differentiation, and interacts with HDACs. SMYD3 specifically methylates H3K4, inducing di- and tri-methylation, but not monomethylation. The related SMYD2 methylates p53 and RB1, as well as H3K4 and H3K36.

The human SUV proteins are homologs of the *Drosophila* Su(var) proteins. There are two homologs, SUV39H1 and SUV39H2, which specifically trimethylate H3K9 after it has already been monomethylated. Both proteins contain N-terminal chromatin organization modifier (chromo) domains, which facilitate the condensation of heterochromatin.[4] They function mainly in these condensed heterochromatin regions, suppressing gene expression. Trimethylation on H3K9 facilitates DNA methylation in this context. Two additional Su(var) homologs, SUV420H1 and SUV420H2, specifically trimethylate H4K20. Like the SUV39 homologs, these proteins are targeted to heterochromatin and are involved in epigenetic transcriptional repression.

Another structurally-defined family, the PRDM series, contains a PR domain, an evolutionarily conserved region of about 100 amino acids that is involved in protein-protein interactions. PRDM proteins also contain classical C2H2-type zinc finger domains which mediate DNA binding. PRDM1, also known as BLIMP1, acts as a transcriptional repressor, binding to the promoter of β-interferon, and in this way regulates B cell maturation. PRDM2, also known as RIZ, is another important family member. It methylates H3K9, binds the retinoblastoma protein, and is highly expressed in brain tumors.

The Enhancer of zeste homologs, EZH1 and EZH2, are polycomb group (PcG) proteins that can mono-, di- and trimethylate H3K27. The EZH proteins contain WD repeat binding domains, which mediate interaction with EED (embryonic ectoderm development) protein to form, with SUZ12 (suppressor of zeste 12 homolog), the polycomb repressor complex 2 (PRC2).[5] Both EZH complexes play important roles in embryonic stem cell function.

A diverse group of SET domain-containing proteins is denoted as SETD. Two key members, SETD1A and SETD1B, methylate H3K4, but not if H3K9 is already methylated. Both proteins, which function as components of multimeric complexes, contain RNA binding domains (RBD). SETD2, unlike the SET1 proteins, methylates H3K36, binds DNA at promoters, and directly binds hyperphosphorylated RNA polymerase II large subunit. This latter interaction is mediated by a Set2Rpb1 interacting (SRI) domain and serves to couple H3K36 methylation with transcript elongation.

Thus, KMTs do not simply generate a methyl mark. All are involved in reading the nucleosomal setting, some requiring methylated marks in order to function. Others facilitate multiple changes, including adding or subtracting marks in addition to the methyl groups that it adds.

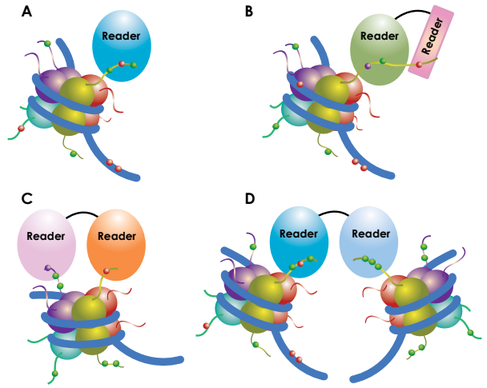



**Figure 2.**
Readers of nucleosomal marks may work alone (A), in combination on a given site (*cis*, B), in pairs on distinct intranucleosomal sites (*trans*, C), or in pairs on different internucleosomal targets (*trans*, D).

| KATs | Target | KMTs |
|---|---|---|
| | H3K4 | ASH1L, MLL, MLL2, MLL3, MLL4, MLL5, SET1A, SET1B, SET5, SET7/9, SETMAR, SMYD1, SMYD2, SMYD3, WHSC1L1 |
| ELP3, GCN5, MYST3, PCAF | H3K9 | EHMT1, EHMT2, EZH2, SETDB1, SETDB2, SUV39H1, SUV39H2 |
| CBP, CLOCK, P300, GCN5, GTF3C4, MYST2, MYST3, NCOA1, TAF1 | H3K14 | |
| CBP, ELP3, P300 | H3K18 | |
| CBP, P300 | H3K27 | EHMT2, EZH1, EZH2, WHSC1, WHSC1L1 |
| | H3K36 | ASH1L, MLL5, NSD1, SET2, SETMAR, SMYD2, WHSC1 |
| CBP, P300, GCN5 | H3K56 | EHMT2 |
| | H3K79 | DOT1L |
| CBP, P300, GCN5, HAT1, MYST2, TIP60 | H4K5 | |
| CBP, P300, GCN5, MYST2, TIP60 | H4K8 | |
| CBP, P300, GCN5, HAT1, MYST2, TIP60 | H4K12 | |
| CBP, P300, GCN5, MYST1, TIP60 | H4K16 | |
| | H4K20 | SET8, SUV420H1, SUV420H2, WHSC1 |
| GCN5 | H4K61 | H3K36me |

**Table 2. Known HATs and KMTs of select H3, H4 lysine residues**

## The Language of Lysine Methylation

In languages, meaning comes from combinations of letters or words. In the language of epigenetics, the message produced by chromatin remodeling enzymes may also be read as groups of marks. Inspection of the N-terminal tails of histones reveals that many of the residues that may be modified with negatively-charged phosphorylation marks are adjacent to lysines, whose charge may have been altered by acetylation. Remarkably, a recent report found that, in histones from *Plasmodium*, the majority of phosphorylation marks were found adjacent to acetylated lysines.[6] This suggests a language 'rule' that pairs these marks together. Another observation comes from organizing histone targets according to the KATs and KMTs which modify them (Table 2). Certain targets (H3K9, H3K27, and H3K56) can be modified by either type of enzyme, indicating these sites may be controlling the message. This becomes more interesting if, as commonly thought, the rate of acetylation/deacetylation is fast while methylation/demethylation is slow.[7,8] Moreover, it is possible that di- and trimethylation differ in stability compared to monomethylation and, as a result, may be functionally distinct, perhaps acting as punctuation (*e.g.*, stop) marks. It should be noted that the information in Table 2 reflects currently known enzyme-target assignments and dramatically underestimates the marks detected by proteomic analysis of histones. Such analyses, compiled at sites like PhosphoSitePlus, reveal that the majority of lysine residues on histones which can be targeted by KATs or KMTs are, in fact, modified by both.

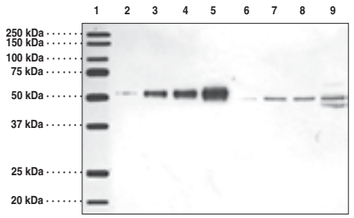
Of course, the message of the marks depends on the readers. Just as nucleosomal marks should not be expected to function in isolation, binding proteins (readers) may assemble together.[9] Readers of nucleosomal marks may work alone, in combination on a given site (*cis*), or in pairs on distinct intranucleosomal sites or on different internucleosomal targets (*trans*), as shown in Figure 2. Since readers serve to recruit or stabilize other proteins at the nucleosome, the interactions between different readers may be indirect, involving associated proteins. In this way, clusters of marks at distant sites may act together to create a complex message.

For article references see page 64

## SET7/9 (FL) Polyclonal Antibody 13780

*KMT7, SETD7/9, SET Domain-Containing Protein*
Protein A-purified IgG **Stability:** ≥1 year at -20°C
**Summary:** Antigen: human recombinant SET7/9 (amino acids 1-366) • Host: rabbit • Cross Reactivity: (+) human and mouse SET7/9 • Application(s): WB • SET7/9 is a histone specific HMTase that methylates histone H3 lysine 4.

500 µl

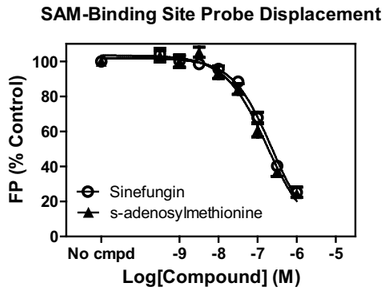



Lane 1: Standard
Lane 2: SET7/9 Recombinant Protein (0.001 µg)
Lane 3: SET7/9 Recombinant Protein (0.005 µg)
Lane 4: SET7/9 Recombinant Protein (0.01 µg)
Lane 5: SET7/9 Recombinant Protein (0.1 µg)
Lane 6: K562 cell lysate (15 µg)
Lane 7: K562 cell lysate (30 µg)
Lane 8: K562 cell lysate (50 µg)
Lane 9: HeLa cell lysate (50 µg)

## SET7/9 SAM-Screener™ Assay Kit 600490

*SET7/9 SAM-Binding Site Inhibitor Screening*
**Stability:** ≥6 months at -80°C **Z' Factor:** 0.71
**Summary:** SET7/9 (KMT7) is a SET domain-containing mono-methyltransferase that acts on a large number of histone and non-histone targets including histone H3, TAF10, p53, viral Tat, and estrogen receptor α. This fluorescence polarization assay is based upon a proprietary small molecule fluorescent probe that binds to the SAM binding pocket in SET7/9. Binding of the small molecule probe to SET7/9 induces an increase in fluorescence polarization. Binding of the probe can be competed with the endogenous cofactor SAM or by the inhibitor sinefungin, but is unaffected by the histone H3 peptide substrate. The SET7/9 SAM-Screener Assay is robust and exhibits a greater than 100 mP shift over a range of 0-250 nM SET7/9. The assay is suitable for high-throughput screening in the provided 384-well plate or can be scaled to higher density plate formats (*e.g.*, 1,536-well) if desired.

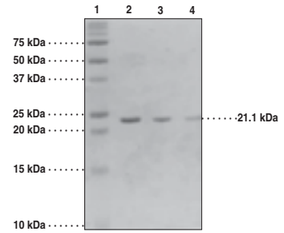
384 wells
1,920 wells




## SET8 (human recombinant) 10319

*KMT5a, PR-Set7, SETD8, SET domain-containing (lysine methyltransferase) 8*
**$M_r$:** 21.1 kDa **Purity:** ≥95% **Stability:** ≥6 months at -80°C
**Source:** Active recombinant N-terminal His-tagged protein amino acids 190-352 expressed in *E. coli* • SET8 selectively mono-methylates histone H4 at lysine 20, an event proven to have an important role in chromatin structure and transcriptional activation. SET8 is also a novel regulator of p53, mono-methylating lysine 382 of the tumor suppressor. SET8's ability to suppress p53 transcriptional activity implies that it may play a significant role in tumorigenesis.

25 µg
50 µg
100 µg

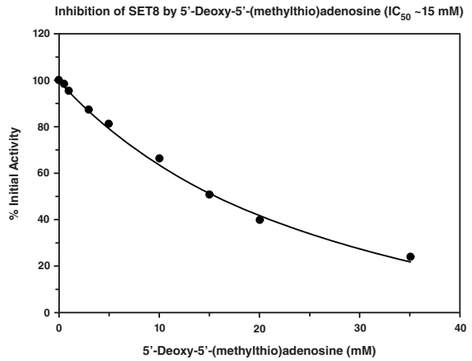



Lane 1: MW Markers
Lane 2: SET8 (4 µg)
Lane 3: SET8 (2 µg)
Lane 4: SET8 (1 µg)

## SET8 Methyltransferase Inhibitor Screening Assay Kit 700350

**Stability:** ≥6 months at -80°C
**Summary:** SET8 is a methyltransferase that selectively mono-methylates H4K20, an event proven to have an important role in chromatin structure and transcriptional activation. Cayman's SET8 Methyltransferase Inhibitor Screening Assay provides a convenient method for screening human SET8 inhibitors. The transfer of the methyl group from SAM by SET8 (provided in the kit) to the acceptor peptide (H4K20) generates SAH, which is rapidly converted to urate and $H_2O_2$ using an enzyme mixture provided in the kit. The $H_2O_2$ formed is quantified using ADHP to produce the highly fluorescent compound resorufin (excitation 530-540 nm; emission 585-595 nm).

96 wells

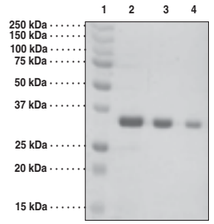





## SETD2 (human recombinant) 10767

*Huntington Interacting Protein B, HYPB, KMT3A, p231HBP*
**$M_r$:** 33.7 kDa **Purity:** ≥95% **Stability:** ≥9 months at -80°C
**Source:** Active recombinant N-terminal His-tagged protein consisting of amino acids 1,435-1,711 expressed in *E. coli* • SETD2 is a histone methyltransferase that catalyzes the trimethylation of H3K36. The WW domain of SETD2 has been shown to interact with hyperphosphorylated RNA polymerase II, indicating a broad role in transcriptional regulation. Evidence has also been found indicating SETD2 can automethylate itself, possibly influencing its methyltransferase activity.

25 µg
50 µg
100 µg

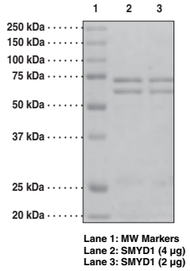



Lane 1: MW Markers
Lane 2: SETD2 (5 µg)
Lane 3: SETD2 (2.5 µg)
Lane 4: SETD2 (1 µg)

## SMYD1 (human recombinant) 10761

*SET and MYND domain-containing protein 1, smk-BOP*
**$M_r$:** 69.6 kDa **Purity:** ≥50% **Stability:** ≥9 months at -80°C
**Source:** Active recombinant N-terminal His- and SUMOpro-tagged protein consisting of amino acids 2-490 expressed in *E. coli* • SMYD1 is a cardiac and muscle-specific histone methyltransferase, specifically methylating H3K4, and is crucial for cardiomyocyte differentiation and maturation.

10 µg
25 µg
50 µg



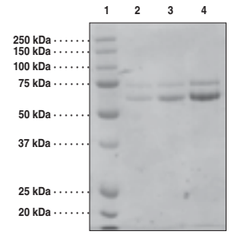

Lane 1: MW Markers
Lane 2: SMYD1 (4 µg)
Lane 3: SMYD1 (2 µg)

*NOTE: SUMO Affinity tag used under license from LifeSensors, Inc.*

## SMYD3 (human recombinant) 10762

*KMT3E, SET and MYND domain-containing protein 3*
**$M_r$:** 58.5 kDa **Purity:** ≥60% **Stability:** ≥9 months at -80°C
**Source:** Active recombinant N-terminal His- and SUMOpro-tagged protein consisting of amino acids 35-428 expressed in *E. coli* • SMYD3 is a histone methyltransferase that is overexpressed in several different cancers, such as breast, colorectal, and liver cancer. The N-terminus of full-length SMYD3 interacts with Hsp90α and increases its activity, suggesting that the N-terminal region is involved in regulating methyltransferase activity.

10 µg
25 µg
50 µg



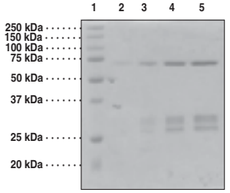

Lane 1: MW Markers
Lane 2: SMYD3 (1 µg)
Lane 3: SMYD3 (2 µg)
Lane 4: SMYD3 (5 µg)

*NOTE: SUMO Affinity tag used under license from LifeSensors, Inc.*

## SUV4-20H1 (human recombinant) 10763

*KMT5B, Lysine N-methyltransferase 5B, Suppressor of Variegation 4-20 Homolog 1*
**$M_r$:** 70.7 kDa **Purity:** ≥60% **Stability:** ≥6 months at -80°C
**Source:** Active recombinant N-terminal GST-tagged protein consisting of amino acids 2-387 expressed in *E. coli* • SUV4-20H1 is a SET domain containing methyltransferase responsible for di- and trimethylation of histone H4 lysine 20 (H4K20me2 and H4K20me3) at pericentric heterochromatin.

25 µg
50 µg
100 µg

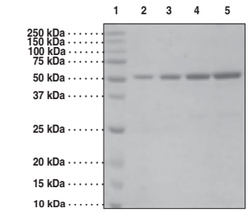



Lane 1: MW Ladders
Lane 2: KMT5B (0.5 µg)
Lane 3: KMT5B (1 µg)
Lane 4: KMT5B (2 µg)
Lane 5: KMT5B (4 µg)

## SUV4-20H2 (human recombinant) 10764

*KMT5C, Suppressor of Variegation 4-20 Homolog 2*
**$M_r$:** 58.6 kDa **Purity:** ≥95% **Stability:** ≥6 months at -80°C
**Source:** Active recombinant N-terminal GST-tagged protein consisting of amino acids 2-280 expressed in *E. coli* • SUV4-20H2 is a SET domain containing methyltransferase responsible for di- and trimethylation of histone H4 lysine 20 (H4K20me2 and H4K20me3) at pericentric heterochromatin.

25 µg
50 µg
100 µg




Lane 1: MW Ladder
Lane 2: KMT5C (1 µg)
Lane 3: KMT5C (2 µg)
Lane 4: KMT5C (4 µg)
Lane 5: KMT5C (6 µg)

## TAF10 Peptide 10228

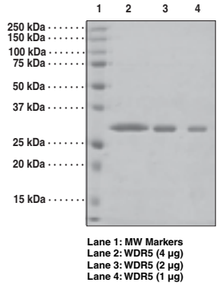
*TAB-Associated Factor 10, TAFII30, TAF10 RNA polymerase II, TATA Box Binding Protein (TBP)-Associated Factor*
**FW:** 1,267.0 **Supplied as:** 1 mg peptide lyophilized peptide from bicarbonate buffer
**Stability:** ≥1 year at -20°C
**Summary:** TAF10 is one of many protein factors or coactivators associated with RNA polymerase II activity. One vial of this peptide may be used as a methyltransferase acceptor peptide for more than 200 reactions at 15 µM.

1 ea

## WDR5 (human recombinant) 10944

*BIG3, BMP2-induced 3-kb Gene Protein, SSET1c WD40 Repeat Protein, SWD3, WD-Repeat Protein 5*
**$M_r$:** 34.4 kDa **Purity:** ≥95% **Stability:** ≥6 months at -80°C
**Source:** Recombinant protein consisting of amino acids 23-334 expressed in *E. coli* • WDR5 has been demonstrated to bind histone H3 by recognizing the first three amino acids of the N-terminal tail. Binding of WDR5 to a conserved arginine-containing motif in MLL-1, the so-called WDR5 interaction ("Win") motif, promotes the assembly and activity of the MLL core complex.

50 µg
100 µg
250 µg



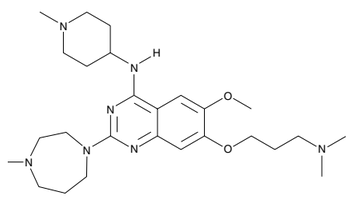
Lane 1: MW Markers
Lane 2: WDR5 (4 µg)
Lane 3: WDR5 (2 µg)
Lane 4: WDR5 (1 µg)

*NOTE: SUMO Affinity tag used under license from LifeSensors, Inc.*

## UNC0224 13631

*[1197196-48-7]*
**MF:** $C_{26}H_{43}N_7O_2$ **FW:** 485.7 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** A potent and selective G9a HMTase inhibitor ($IC_{50}$ = 15 nM; $K_d$ = 23 mM); more than 1,000-fold selective for G9a over SET7/9 and SET8

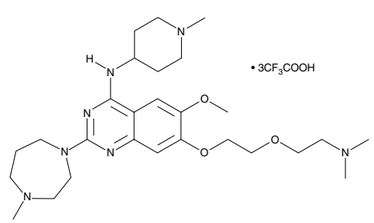
1 mg
5 mg
10 mg
50 mg



## UNC0321 (trifluoroacetate salt) 10582

**MF:** $C_{27}H_{45}N_7O_3 \bullet 3(CF_3COOH)$ **FW:** 857.8 **Purity:** ≥95%
A solution in methyl acetate **Stability:** ≥1 year at -20°C
**Summary:** A potent and selective G9a HMTase inhibitor ($IC_{50}$ = 6 nM; $K_i$ = 63 pM); more than 40,000-fold selective for G9a over SET7/9, SET8, PRMT3, and JMJD2E

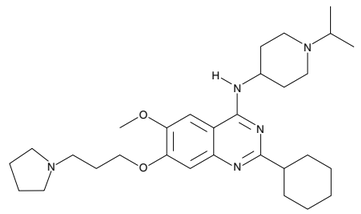
1 mg
5 mg
10 mg
25 mg




## UNC0638 10734

*[1255580-76-7]*
**MF:** $C_{30}H_{47}N_5O_2$ **FW:** 509.7 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** A potent, selective G9a and GLP HMTase inhibitor ($IC_{50}$s = <15 and 19 nM, respectively); inhibits H3K9 dimethylation in MDA-MB231 cells ($IC_{50}$ = 81 nM) and demonstrates favorable separation of functional and toxic effects

1 mg
5 mg
10 mg
25 mg







# Demethylases

## Antibodies



## Biochemicals



## Kits



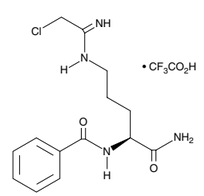
## Proteins



## Cl-Amidine 10599

*[913723-61-2]*
**MF:** $C_{14}H_{19}ClN_4O_2 \bullet CF_3CO_2H$ **FW:** 424.8 **Purity:** ≥95%
A crystalline solid **Stability:** ≥1 year at -20°C
**Summary:** An inhibitor of PAD4 deimination activity ($IC_{50}$ = 5.9 µM) that also inhibits PAD1 and PAD3 ($IC_{50}$ = 0.8 and 6.2 µM, respectively); dose dependently decreases the citrulline content in serum and joints and reduces the development of IgG autoantibodies in a CIA mouse model of inflammatory arthritis

1 mg
5 mg
10 mg
50 mg

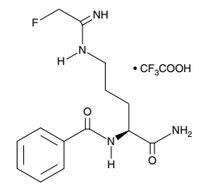



*NOTE: Sold under license from University of South Carolina under U.S. Patent No. 7,964,363*

## F-Amidine (trifluoroacetate salt) 10610

*[877617-46-4]*
**MF:** $C_{14}H_{19}FN_4O_2 \bullet CF_3COOH$ **FW:** 408.4 **Purity:** ≥95%
A solution in methanol **Stability:** ≥1 year at -20°C
**Summary:** Inhibits PAD4 activity ($IC_{50}$ = 21.6 µM) as well as PAD1 and PAD3 activity ($IC_{50}$s = 29.5 and 350 µM, respectively); cytotoxic to HL-60, MCF7, and HT-29 cancer cell lines ($IC_{50}$s = 0.5, 0.5 and 1 µM, respectively)

100 µg
250 µg
500 µg
1 mg

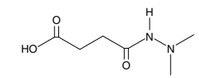



*NOTE: Sold under license from University of South Carolina under U.S. Patent No. 7,964,363*

## Daminozide 12033

*[1596-84-5] Alar, Aminozide, B 995, DIMG, DMASA, Kylar, SADH, Succinic Acid*
**MF:** $C_6H_{12}N_2O_3$ **FW:** 160.2 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** A selective inhibitor of the human 2-oxoglutarate (JmjC) histone demethylases KDM2A, PHF8, and KDM7A ($IC_{50}$s = 1.5, 0.55, and 2.1 µM, respectively)

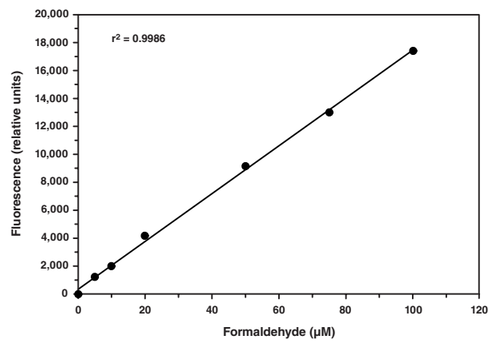
5 g
10 g
25 g



## Demethylase (Jumonji-type) Activity Assay Kit 700390

**Stability:** ≥6 months at -80°C
**Summary:** Lysine demethylases containing Jumonji C (JmjC) domains produce formaldehyde following 2-oxoglutarate-dependent demethylation. Cayman's Demethylase (Jumonji-type) Activity Assay provides a convenient fluorescence-based method for assaying JmjC-mediated demethylase activity from cell lysates or purified enzyme preparations. The assay is based on the production of formaldehyde during the demethylation of a methylated peptide substrate. Cyclization of formaldehyde and acetoacetanilide in the presence of ammonia gives a fluorescent product for quantitation.

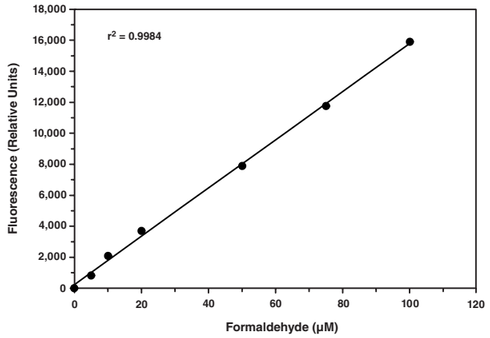
96 wells



## Demethylase (LSD-type) Activity Assay Kit 700400

**Stability:** ≥6 months at -80°C
**Summary:** Cayman's Demethylase (LSD-type) Activity Assay provides a fluorescence-based method for assaying LSD-type demethylase activity. In this assay, formaldehyde is measured directly, eliminating the need for a coupled-enzyme reaction system. Formaldehyde, produced during demethylation of lysine 4 on a histone H3 peptide, reacts with the detection reagents provided in the kit to give a brightly fluorescent product. The assay is easy to use and can be completed in under two hours.

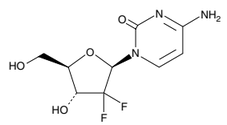
96 wells




## Gemcitabine 11690

*[95058-81-4] DDFC, Folfugem, Gemcel, GemLip, Gemzar, LY 188011, NSC 613327, Zefei*
**MF:** $C_9H_{11}N_3O_4F_2$ **FW:** 263.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** A nucleoside analog that arrests tumor growth and induces apoptosis by inhibiting DNA replication and repair; inhibits repair-mediated DNA demethylation inducing epigenetic gene silencing and has broad antiretroviral activity

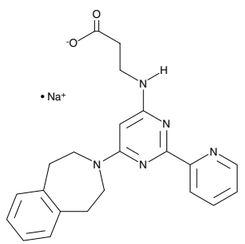
10 mg
25 mg
50 mg
100 mg




## GSK-J1 (sodium salt) 12054

**MF:** $C_{22}H_{22}N_5O_2$ • Na **FW:** 411.4 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** A potent, cell impermeable H3K27 histone demethylase inhibitor highly selective for human JMJD3 ($IC_{50}$ = 60 nM *in vitro*)

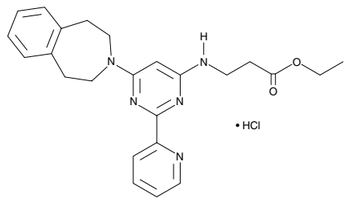
1 mg
5 mg
10 mg
50 mg




## GSK-J4 (hydrochloride) 12073

**MF:** $C_{24}H_{27}N_5O_2$ • HCl **FW:** 454.0 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** An ethyl ester prodrug of the JMJD3 selective histone demethylase inhibitor GSK-J1; reduces LPS-induced proinflammatory cytokine production, including that of TNFα ($IC_{50}$ = 9 µM) in human primary macrophages

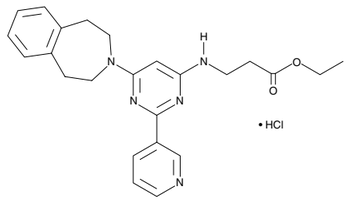
1 mg
5 mg
10 mg
50 mg




## GSK-J5 (hydrochloride) 12074

**MF:** $C_{24}H_{27}N_5O_2$ • HCl **FW:** 454.0 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** A pyridine regio-isomer of the JMJD3 inhibitor GSK-J4; cell-permeable and hydrolyzed to a free base, which is a weak inhibitor of JMJD3 ($IC_{50}$ = 100 µM), making it an ideal negative control molecule

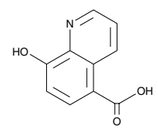
1 mg
5 mg
10 mg




## IOX1 11572

*[5852-78-8]*
**MF:** $C_{10}H_7NO_3$ **FW:** 189.2 **Purity:** ≥97%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** A broad-spectrum inhibitor of 2OG oxygenases that inhibits JMJD2 demethylase activity ($IC_{50}$ = 87 µM); inhibits JMJD2A, JMJD2E and the 2OG oxygenases PHF8, PHD2, and FIH ($IC_{50}$s = 1.7, 2.4, 13.3, 14.3, and 20.5 µM, respectively)

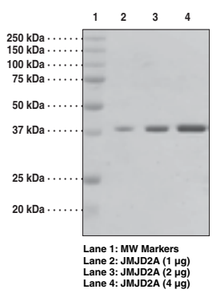
1 mg
5 mg




## JMJD2A (human recombinant) 10336

*JHDM3A, Jumonji Domain Containing 2A, KDM4A*
**$M_r$:** 42.7 kDa **Purity:** ≥95% **Stability:** ≥6 months at -80°C
**Source:** Active recombinant N-terminal His-tagged protein consisting of amino acids 1-350 expressed in *E. coli* • JMJD2A catalyzes the demethylation of tri- and di-methylated forms of histone H3 at lysine residues 9 and 36.

25 µg
50 µg
100 µg




Lane 1: MW Markers
Lane 2: JMJD2A (1 µg)
Lane 3: JMJD2A (2 µg)
Lane 4: JMJD2A (4 µg)

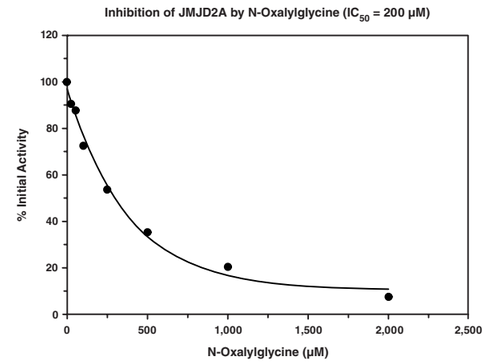




## JMJD2A Inhibitor Screening Assay Kit 700360

*Jumonji Domain Containing 2A, KDM4A*
**Stability:** ≥6 months at -80°C
**Summary:** JMJD2A is a JmjC histone demethylase that catalyzes the demethylation of trimethylated lysine 9 and lysine 36 of histone H3. Cayman's JMJD2A Inhibitor Screening Assay Kit provides a convenient fluorescence-based method for screening JMJD2A inhibitors. The assay is based on the multistep reaction in which JMJD2A first produces formaldehyde during the demethylation of the trimethylated peptide substrate, histone H3 trimethyl lys9, with the concomitant oxidation/decarboxylation of 2-oxoglutarate. The detection reaction involves the cyclization between formaldehyde and acetoacetanilide in the presence of ammonia. The resulting fluorescent product is analyzed using an excitation wavelength between 365-375 nm and an emission wavelength between 465-475 nm.

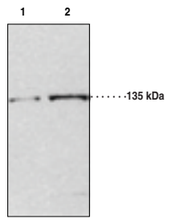
96 wells




## JMJD2A Polyclonal Antibody 10382

*Jumonji Domain Containing 2A, KDM4A, Lysine-Specific Demethylase 4A*
Antigen affinity-purified IgG **Stability:** ≥1 year at -20°C
**Summary:** Antigen: recombinant human JMJD2A amino acids 1-350 • Cross Reactivity: (+) human JMJD2A • Application(s): WB • JMJD2A is a lysine specific demethylase with emerging roles in histone modification or epigenetic remodeling. This JMJD2A polyclonal antibody was raised against an N-terminal recombinant fragment of JMJD2A. This fragment (amino acids 1-350) includes the JMJN and JMJC domains but not the two LAP/PHD zinc finger or Tudor domains of the 1,064 amino acid protein.

1 ea

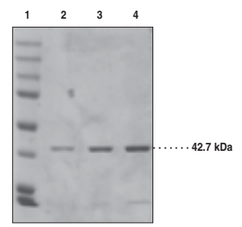



Lane 1: DLD1 cell lysate (30 µg)
Lane 2: DLD1 cell lysate (60 µg)

## JMJD2A-Strep tagged (human recombinant) 11299

*JHDM3A, Jumonji Domain Containing 2A, KDM4A*
**$M_r$:** 42.7 kDa **Purity:** ≥95% **Stability:** ≥6 months at -80°C
**Source:** Active recombinant N-terminal Strep II-tagged protein consisting of amino acids 2-350 expressed in *E. coli* • JMJD2A catalyzes the demethylation of trimethylated forms of histone at lysine residues 9 and 36. JMJD2A is an α-ketoglutarate-dependent Fe (II) oxygenase. Purification of Fe-dependent JmjC family members by IMAC can result in displacement of the catalytic iron and decreased activity. Therefore this protein is purified by Strep-Tactin affinity chromatography.

25 µg
50 µg
100 µg

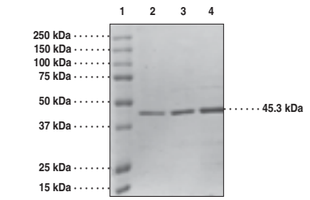



Lane 1: MW Markers
Lane 2: JMJD2A (2 µg)
Lane 3: JMJD2A (4 µg)
Lane 4: JMJD2A (6 µg)

## JMJD2C-Strep tagged (human recombinant) 10776

*JMJCD3C , Jumonji Domain Containing 2C , KDM4C, KIAA0780 , Lysine-specific Demethylase 4C*
**$M_r$:** 45.3 kDa **Purity:** ≥90% **Stability:** ≥6 months at -80°C
**Source:** Active recombinant N-terminal Strep II-tagged protein consisting of amino acids 2-372 expressed in *E. coli* • JMJD2C catalyzes the demethylation of trimethylated histone H3 at lysine residues 9 or 36 (me 2/3), leading to transcriptional changes. JMJD2C is an α-ketoglutarate-dependent Fe (II) oxygenase. Purification of Fe-dependent JmjC family members by IMAC can result in displacement of the catalytic iron and decreased activity. Therefore this protein is purified by Strep-Tactin affinity chromatography.

25 µg
50 µg
100 µg

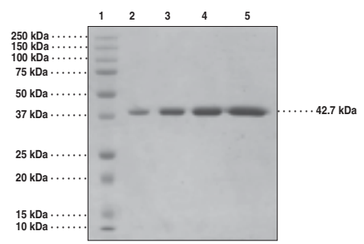



Lane 1: MW Markers
Lane 2: JMJD2C (1 µg)
Lane 3: JMJD2C (2 µg)
Lane 4: JMJD2C (4 µg)

## JMJD2D (human recombinant) 10335

*Jumonji Domain Containing 2D, KDM4D, Lysine-Specific Demethylase 4D*
**$M_r$:** 42.7 kDa **Purity:** ≥75% **Stability:** ≥6 months at -80°C
**Source:** Active recombinant N-terminal His-tagged protein consisting of amino acids 1-354 expressed in *E. coli* • JMJD2D catalyzes the demethylation of di- and trimethylated forms of histone H3 at lysine residue 9 (me2/3), leading to transcriptional repression and activation, respectively.

25 µg
50 µg
100 µg

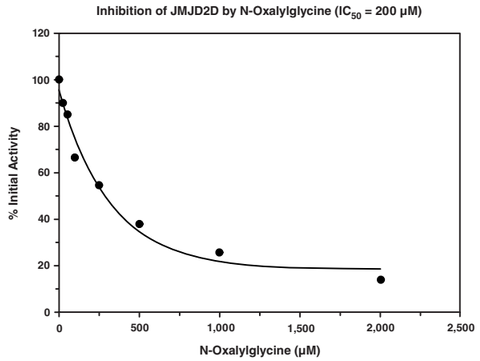



Lane 1: MW ladder
Lane 2: JMJD2D (1 µg)
Lane 3: JMJD2D (2 µg)
Lane 4: JMJD2D (4 µg)
Lane 5: JMJD2D (6 µg)

## JMJD2D Inhibitor Screening Assay Kit 700370

*Jumonji Domain Containing 2D*
**Stability:** ≥6 months at -80°C
**Summary:** JMJD2D is a JmjC histone demethylase that catalyzes the demethylation of di- and trimethylated lysine 9 of histone H3. Cayman's JMJD2D Inhibitor Screening Assay Kit provides a convenient fluorescence-based method for screening JMJD2D inhibitors. The assay is based on the multistep reaction in which JMJD2D first produces formaldehyde during the demethylation of the trimethylated peptide substrate, histone H3 trimethyl lysine 9, with the concomitant oxidation/decarboxylation of 2-oxoglutarate. The detection reaction involves the cyclization between formaldehyde and acetoacetanilide in the presence of ammonia. The resulting fluorescent product is analyzed using an excitation wavelength between 365-375 nm and an emission wavelength between 465-475 nm.

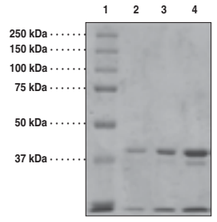
96 wells




## JMJD2D-Strep tagged (human recombinant) 11300

*Jumonji Domain Containing 2D, KDM4D, Lysine-specific Demethylase 4D*
**$M_r$:** 42.6 kDa **Purity:** ≥70% **Stability:** ≥6 months at -80°C
**Source:** Active recombinant N-terminal Strep II-tagged protein consisting of amino acids 4-354 expressed in *E. coli* • JMJD2D catalyzes the demethylation of di- and trimethylated forms of histone H3 at lysine residue 9 (me2/3), leading to transcriptional repression and activation, respectively. JMJD2D is an α-ketoglutarate-dependent Fe (II) oxygenase. Purification of Fe-dependent JmjC family members by IMAC can result in displacement of the catalytic iron and decreased activity. Therefore this protein is purified by Strep-Tactin affinity chromatography.

25 µg
50 µg
100 µg

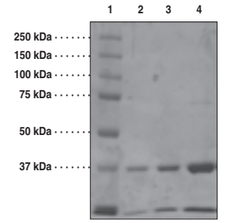



Lane 1: MW Markers
Lane 2: JMJD2D (2.5 µg)
Lane 3: JMJD2D (5 µg)
Lane 4: JMJD2D (10 µg)

## JMJD2E-Strep tagged (human recombinant) 11237

*Jumonji Domain Containing 2E, KDM4D-Like*
**$M_r$:** 40.8 kDa **Purity:** ≥75% **Stability:** ≥6 months at -80°C
**Source:** Active recombinant N-terminal Strep II-tagged protein consisting of amino acids 2-337 expressed in *E. coli* • JMJD2E catalyzes the demethylation of histone H3 at lysine residue 9. JMJD2E is an α-ketoglutarate-dependent Fe (II) oxygenase. Purification of Fe-dependent JmjC family members by IMAC can result in displacement of the catalytic iron and decreased activity. Therefore this protein is purified by Strep-Tactin affinity chromatography.

25 µg
50 µg
100 µg

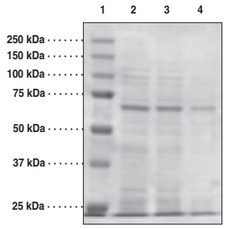



Lane 1: MW Markers
Lane 2: JMJD2E (2.5 µg)
Lane 3: JMJD2E (5 µg)
Lane 4: JMJD2E (10 µg)

## JMJD6 (human recombinant) 10773

*Jumonji Domain Containing 6, KIAA0585, PTDSR1*
**$M_r$:** 73.2 kDa **Purity:** ~50% **Stability:** ≥6 months at -80°C
**Source:** Recombinant N-terminal GST-tagged protein consisting of amino acids 2-403 expressed in *E. coli* • JMJD6 was initially proposed to function as a histone arginine demethylase. Further studies suggest that JMJD6 has hydroxylase activity towards histone tails, the splicing regulatory protein LUC7-Like2, or single-stranded RNA.

25 µg
50 µg
100 µg




Lane 1: MW Markers
Lane 2: JMJD6 (6 µg)
Lane 3: JMJD6 (4 µg)
Lane 4: JMJD6 (2 µg)

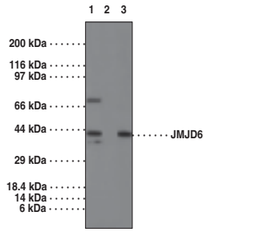




## JMJD6 Peptide Affinity-Purified Polyclonal Antibody 13787

*Jumonji Domain Containing 6, PTDSR*
Antigen affinity-purified IgG **Stability:** ≥1 year at -20°C
**Summary:** Antigen: human JMJD6 amino acids 127-144 • Host: rabbit • Cross Reactivity: (+) chimpanzee, ovine, canine, equine, human, mouse, and opossum JMJD6 • Application(s): WB • JMJD6 is a 403 amino acid nuclear protein lysyl-hydroxylase that has been reported to have arginine demethylase activity for histone H3 at 'Arg-2' and histone H4 at 'Arg-3'. JMJD6 has been suggested to function in the differentiation of multiple organs during embryogenesis and regulate hematopoietic differentiation and macrophage cytokine responses.

1 ea

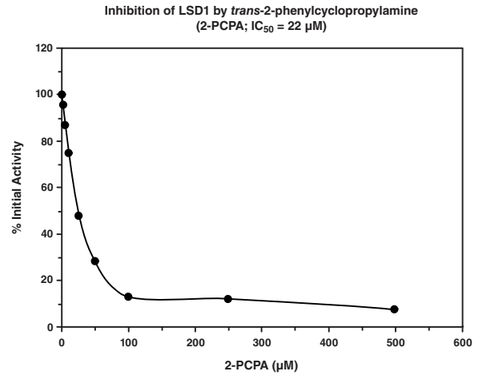



Lane 1: Human brain lysate (Absence of immunizing peptide)
Lane 2: Human brain lysate (Presence of immunizing peptide)
Lane 3: Mouse brain lysate

## LSD1 Inhibitor Screening Assay Kit 700120

*Lysine-Specific Demethylase 1*
**Stability:** ≥6 months at -80°C
**Summary:** LSD1 is a histone demethylase whose actions on specific lysine residues repress transcription of chromosomal DNA. LSD1 also inhibits the tumor suppressor activity of p53 by demethylating a specific lysine residue. Cayman's LSD1 Inhibitor Screening Assay Kit provides a convenient fluorescence-based method for screening LSD1-specific inhibitors. The assay is based on the multistep enzymatic reaction in which LSD1 first produces $H_2O_2$ during the demethylation of lysine 4 on a peptide corresponding to the first 21 amino acids of the N-terminal tail of histone H3. In the presence of horseradish peroxidase, $H_2O_2$ reacts with ADHP to produce the highly fluorescent compound resorufin that can be analyzed with an excitation wavelength of 530-540 nm and an emission wavelength of 585-595 nm.

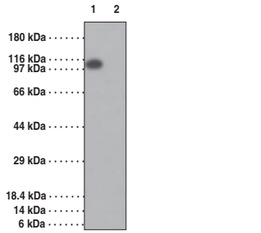
96 wells




## LSD1 Polyclonal Antibody (aa 100-150) 13554

*Amine Oxidase (flavin containing) Domain 2*
Protein affinity-purified IgG **Stability:** ≥1 year at -20°C
**Summary:** Antigen: peptide corresponding to a portion of human LSD1 amino acids 100-150 • Host: rabbit • Cross Reactivity: (+) canine, human, mouse, rat, Rhesus monkey, and zebrafish LSD1 • Application(s): WB • LSD1 functions as a transcriptional corepressor and catalyzes the flavin-dependent demethylation of Lys4 of histone 3 resulting in the formation of methyl-free lysine and release of formaldehyde. It is typically associated with CoREST and HDACs 1 and 4 and participates in the silencing of endogenous neuron-specific genes.

1 ea

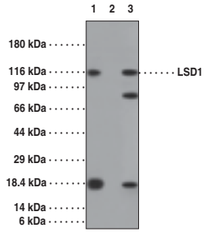



Lane 1: Human brain homogenate
Lane 2: Human brain homogenate-probed with antibody incubated with immunizing peptide

## LSD1 Polyclonal Antibody (aa 400-450) 13553

Protein G-purified IgG **Stability:** ≥1 year at -20°C
**Summary:** Antigen: peptide from a portion of human LSD1 amino acids 400-450 • Host: rabbit • Cross Reactivity: (+) chimpanzee, bovine, canine, human, monkey, and mouse LSD1 • Application(s): WB

1 ea

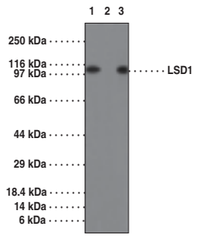



Lane 1: Jurkat cell lysate (absence of blocking peptide)
Lane 2: Jurkat cell lysate (presence of blocking peptide)
Lane 3: NIH 3T3 cell lysate

## LSD1 Polyclonal Antibody (aa 450-500) 13486

Protein G-purified IgG **Stability:** ≥1 year at -20°C
**Summary:** Antigen: peptide within the region of human LSD1 amino acids 450-500 • Host: rabbit • Cross Reactivity: (+) chimpanzee, bovine, canine, equine, human, mouse, orangutan, and porcine LSD1 • Application(s): WB

1 ea




Lane 1: Jurkat cell lysate
Lane 2: Jurkat cell lysate; antibody blocked with immunizing peptide
Lane 3: 3T3 cell lysate

# Histone Demethylation

by [Daniel A. Bochar, Ph.D.]

The alteration of chromatin structure provides a key regulatory step for all processes that act upon DNA. One mechanism for inducing these changes is through the posttranslational modification of histones. Of the multitude of covalent modifications that occur on histones, lysine methylation plays a central role in the epigenetic regulation of the genome.[1] The methylation state of histone residues is dynamically regulated through the opposing activities of histone methyltransferases and demethylases. Histones are methylated on numerous lysine or arginine residues, and to add further complexity, lysine residues may be mono-, di-, or tri-methylated, and arginine residues may be mono-, symmetrically, or asymmetrically di-methylated. Unlike the other common histone modifications of acetylation or phosphorylation, methylation does not alter the charge of the modified residue. Charge alteration of histone can directly impact histone-DNA or histone-histone interactions, suggesting that histone methylation elicits its effect by recruiting or blocking association of chromatin associated factors that can direct relevant activities to appropriate regions of the genome.

The histone modifications of acetylation and phosphorylation are dynamically regulated through opposing enzymatic actions; i.e. acetyltransferases/deacetylases or kinases/phosphatases. Until recently, histone methylation was thought to be a static mark lacking this dynamic relationship. This assumption was based on the high stability of the carbon-nitrogen bond, and therefore removal of the methyl mark was thought to occur only through histone turnover or proteolytic removal of the histone tails.[2] The discovery of enzymes capable of removing this mark has solidified the dynamic nature of histone methylation, and has set the stage for a wide range of biological and pharmacological discoveries.

In 2004, LSD1 was identified as the first histone demethylase.[3] This enzyme, which primarily demethylates H3K4, belongs to a larger family of FAD-dependent amine oxidases. LSD1 catalyzed demethylation occurs through the two electron oxidation of the amine by FAD to produce an iminium ion. This intermediate spontaneously hydrolyzes to produce formaldehyde and a product lysine less one methyl group (Figure 1). It is important to note that formation of the imine intermediate requires free electrons on the epsilon nitrogen and therefore only mono- or di-methylated lysine can serve as a substrate. LSD1 was first identified in the BRAF-HDAC complex along with the transcriptional corepressor, CoREST.[4] This association suggests LSD1-catalyzed demethylation is important for transcriptional repression. Subsequently, LSD1 was identified as an androgen receptor-interacting protein and in this context LSD1 changed substrate specificity to H3K9,[5] suggesting that LSD1 can act as a corepressor or coactivator based on its associated factors. In humans, there exists only one LSD1 paralog, LSD2, and this protein has also been shown to possess histone demethylase activity for H3K4 mono- and di-methyl.[6]

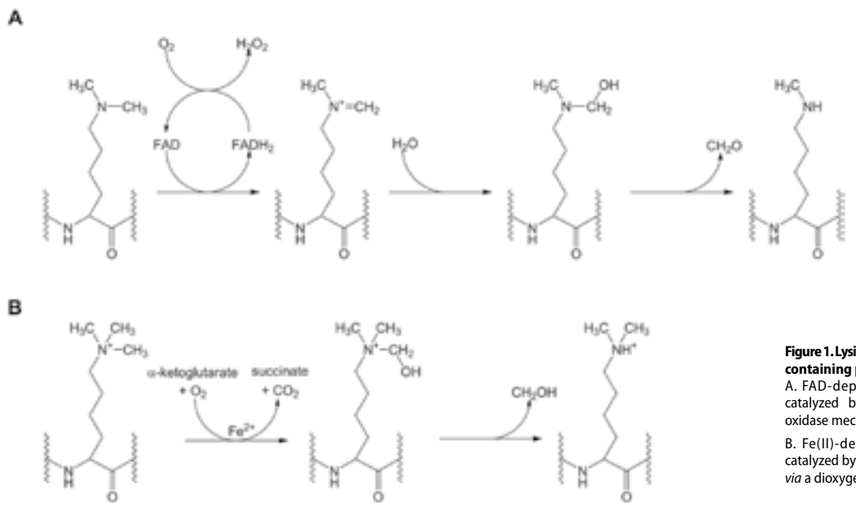



**Figure 1. Lysine demethylation by LSD1 and JmjC containing proteins.**
A. FAD-dependent lysine demethylation catalyzed by LSD1 proceeds *via* an amine oxidase mechanism.

B. Fe(II)-dependent lysine demethylation catalyzed by JmjC containing proteins proceeds *via* a dioxygenase mechanisim.

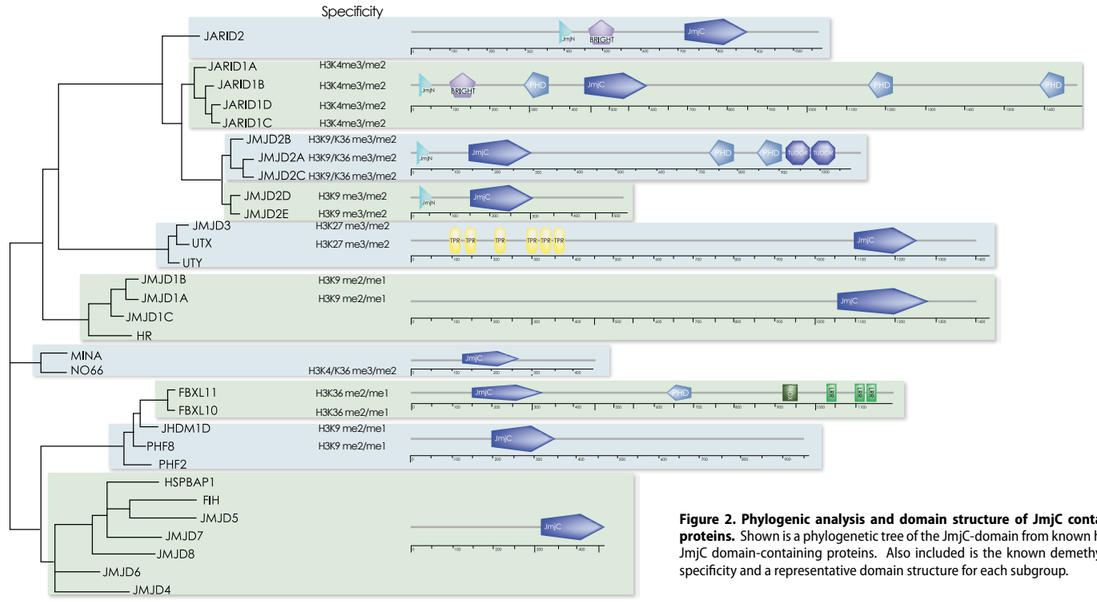



**Figure 2. Phylogenic analysis and domain structure of JmjC containing proteins.** Shown is a phylogenetic tree of the JmjC-domain from known human JmjC domain-containing proteins. Also included is the known demethylation specificity and a representative domain structure for each subgroup.

As shown in Figure 2, not all JmjC domain-containing proteins have an identified substrate. The search for JmjC domain substrates is complicated by the fact that these enzymes may not function as histone demethyases, as illustrated by JMJD6. The enzyme JMJD6 has been shown to be a lysyl hydroxylase catalyzing lysine C-5 hydroxylation of arginine–serine-rich regions of splicing regulatory proteins.[8] The crystal structure of the related JMJD5 suggests that this protein may also function as a lysyl hydroxylase.[9] A third member of this phylogenetic clade, FIH, also functions as a hydroxylase, this time as an asparaginyl hydroxylase targeting the transcription factor HIF1α. Therefore, it is clear that not all JmjC domain-containing proteins will function as histone demethylases and identifying the JmjC domain-containing proteins with epigenetic activity is an area of active research.

Initial comparisons of the catalytic activity of JmjC domain-containing proteins to LSD1 suggest that JmjC domain-containing proteins are over a magnitude lower in activity than that of LSD1.[10] This had initially raised speculation as to whether or not these enzymes are biologically relevant demethylases. Interestingly, JmjC domain-containing proteins are inhibited by divalent transition metals (*e.g.* Ni(II)) that can displace the catalyticly required Fe(II).[11] Common purification schemes for many of the JmjC domain-containing proteins have included metal affinity chromatography, raising the possibility of inhibition of the purified target enzyme. Indeed, metal analysis of metal affinity purified JMJD2A and JMJD2D revealed a Ni(II) content of approximately 70%.[10] In order to avoid identification of a larger, more diverse family of histone demethylases was needed to match the complexity of methyltransferases. A new family of histone demethylases was soon discovered with the characterization of FBXL11 (JHDM1A).[7] This protein was identified following biochemical purification of an H3K36 demethylase activity from HeLa nuclear extracts. FBXL11 was previously uncharacterized, but contained an interesting conserved domain; the Jumonji-C domain (JmjC). The JmjC domain is a member of a larger domain family found in α-ketoglutarate dependent Fe(II) dioxygenases that catalyze a variety of cellular reactions. JmjC-catalyzed demethylation proceeds through the oxidative decarboxylation of α-ketoglutarate coupled to hydroxylation of the methyl group. This hydroxylated intermediate spontaneously decomposes to produce formaldehyde and a product lysine less one methyl group (Figure 1). Unlike LSD1, this mechanism does not require free electrons on the epsilon nitrogen to create an imine intermediate, allowing JmjC demethylases to utilize tri-methylated substrates. Bioinformatic searches of the human genome identify at least 31 JmjC domain-containing proteins, many of which possess histone demethylase activity (Figure 2). The a truly dynamic mark.

Ni(II) contamination, Krishnan, *et. al.* devised a purification strategy utilizing a strep-tag to minimize the exposure to inhibitory transition metals.[10] Using this approach, they demonstrate that the activity of JMJD2A and JMJD2D are approximately equal to that of the LSD1. These results validate the role of JmjC domain-containing proteins in the demethylation of histone substrates.

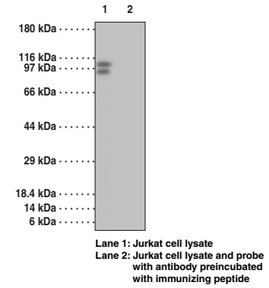
JmjC domain-containing demethylases work in concert with histone methyltransferases to control the methylation patterns of chromatin. These patterning enzymes are important for maintaining normal gene transcription and genomic stability, and disruption of this patterning is seen in many human diseases. One important example is the EZH2/UTX regulation of H3K27 methylation. Overexpression or mutation in EZH2, the histone methyltransferase responsible for this methyl mark, is seen in many prostate and breast cancers.[12] Mutations in UTX, the histone demethylase that removes this mark, have also been described in human cancers.[13] Together, these findings highlight the importance of these balancing enzymes. While there has been a great deal of interest in the development of histone methyltransferase inhibitors as targeted cancer chemotherapeutics, the opposing action of histone demethylases suggests that these enzymes may also represent important drug targets. Indeed, the first selective inhibitor of JmjC domain-containing demethylases was recently described.[14] The discovery of this JMJD3/UTX specific inhibitor demonstrates that JmjC domain-containing demethylases can be selectively inhibited and that this class of enzymes is a tractable area for epigenetic drug discovery. This discovery will hopefully expedite the development of inhibitors for other JmjC domain-containing family members that have been shown to malfunction in human diseases.

For article references see **page 64**

## LSD1 Polyclonal Antibody (aa 800-850) 13555

Protein G-purified IgG **Stability:** ≥1 year at -20°C
**Summary:** Antigen: peptide from human LSD1 within the range of amino acids 800-850 • Host: rabbit • Cross Reactivity: (+) canine, human, mouse, rat, and Rhesus monkey LSD1 • Application(s): IHC (paraffin-embedded sections) and WB

1 ea

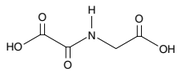


Lane 1: Jurkat cell lysate
Lane 2: Jurkat cell lysate and probe with antibody preincubated with immunizing peptide

## N-Oxalylglycine 13944

*[5262-39-5] NOG*
**MF:** $C_4H_5NO_5$ **FW:** 147.1 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** A cell permeable inhibitor of α-ketoglutarate-dependent enzymes, including JMJD2A, JMJD2C, and JMJD2E ($IC_{50}$s = 250, 500, and 24 µM, respectively); inhibits the prolyl hydroxylase domain-containing proteins PHD1 and PHD2 with $IC_{50}$ values of 2.1 and 5.6 µM, respectively

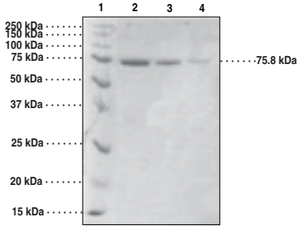
5 mg
10 mg
50 mg
100 mg



## PAD4 (human recombinant) 10500

*Peptidylarginine Deiminase 4, Protein Arginine Deiminase 4*
**$M_r$:** 75.8 kDa **Purity:** ≥95% **Stability:** ≥9 months at -80°C
**Source:** Active recombinant N-terminal His-tagged protein consisting of amino acids 2-663 expressed in *E. coli* • PAD4 is a homodimer that functions as a transcriptional coregulator to catalyze the conversion of specific arginine residues to citrulline in a calcium-dependent manner. PAD4 substrates include histones H2A, H3, and H4, whose post-translational modifications play a large role in gene regulation.

50 µg
100 µg
250 µg

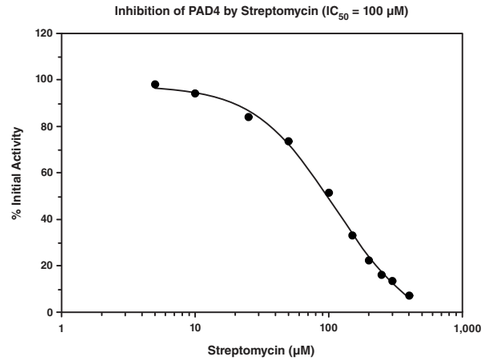


Lane 1: MW Markers
Lane 2: PAD4 (4 µg)
Lane 3: PAD4 (2 µg)
Lane 4: PAD4 (1 µg)

## PAD4 Inhibitor Screening Assay Kit 700560

*Peptidylarginine Deiminase 4, Protein Arginine Deiminase 4*
**Stability:** ≥6 months at -80°C
**Summary:** PAD4 is a guanidino-modifying enzyme that functions as a transcriptional coregulator catalyzing the conversion of specific arginine residues to citrulline. Substrates for PAD4 include histones H2A, H3, and H4. PAD4 autocitrullinates itself at several sites, inhibiting its enzymatic activity. PAD4 activity is increased in rheumatoid arthritis, producing an abundance of citrulline-containing proteins that generate an immune response resulting in production of autoantibodies that ultimately attack the host tissues. PAD4 has also been implicated in several other diseases including multiple sclerosis, Alzheimer's disease, glaucoma, and cancer. Cayman's PAD4 Inhibitor Screening Assay provides a convenient, fluorescence-based method for screening human PAD4 inhibitors.

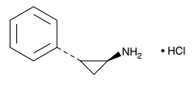
96 wells




## 2-PCPA (hydrochloride) 10010494

*trans-2-Phenylcyclopropylamine, Tranylcypromine*
**MF:** $C_9H_{11}N$ • HCl **FW:** 169.7 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
**Summary:** An irreversible, mechanism-based inhibitor of LSD1 with an $IC_{50}$ value of 20.7 µM and a $K_i$ value of 242 µM that effectively inhibits histone demethylation *in vivo*; irreversibly inhibits monoamine oxidases (MAO) A and MAO B with $IC_{50}$ values of 2.3 and 0.95 µM and $K_i$ values of 101.9 and 16 µM, respectively

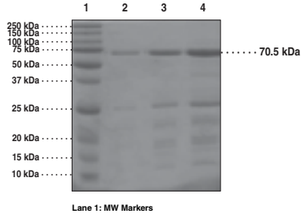
10 mg
50 mg
100 mg
250 mg




## UTX (human recombinant) 10774

*KDM6A, Ubiquitously Transcribed Tetratricopeptide Repeat X*
**$M_r$:** 70.5 kDa **Purity:** ≥85% **Stability:** ≥6 months at -80°C
**Source:** Active recombinant N-terminal proprietary tagged protein consisting of amino acids 930-1,410 expressed in *E. coli* • UTX plays a crucial role in epigenetic regulation of gene expression by catalyzing the demethylation of tri-methylated lysine 27 on histone H3.

25 µg
50 µg
100 µg



Lane 1: MW Markers
Lane 2: UTX (1 µg)
Lane 3: UTX (5 µg)
Lane 4: UTX (10 µg)



# Article References


## DNA Methylation
establishing & editing the methylome
**page 4**

1. Heyn, H., Li, N., Ferreira, H.J., *et al. Proc. Natl. Acad. Sci.* **109,** 10522-10527 (2012).
2. Klose, R.J. and Bird, A.P. *Trends Biochem. Sci.* **31(2),** 89-97 (2006).
3. Clouaire, T., de las Heras, J.I., Merusi, C. *et al. Nucleic Acids Res.* **38(14),** 4620-4634 (2010).
4. Chédin, F., Lieber, M.R., and Hsieh, C.L. *Proc. Natl. Acad. Sci.* **99(26),** 16916-16921 (2002).
5. Kelsey, G. *Cell Res.* **21,** 1155-1156 (2011).
6. Kelsey, G. and Feil, R. *Phil. Trans. R. Soc. B* **368,** 20110336 (2012).
7. Bird, A. *Genes Dev.* **16,** 6-21 (2002).
8. Smallwood, S.A. and Kelsey, G. *Trends Genet.* **28(1),** 33-42 (2012).
9. Pawlak, M. and Jaenisch, R. *Genes Dev.* **25,** 1035-1040 (2011).
10. Ooi, S.K.T., and Bestor, T.H. *Cell* **133,** 1145-1148 (2008).
11. Bhutani, N., Burns, D.M., and Blau, H.M. *Cell* **146,** 866-872 (2011).
12. Yang, X., Lay, F., Han, H. *et al. Trends Pharmacol. Sci.* **31(11),** 536-546 (2010).
13. McCabe, M.T., Brandes, J.C., and Vertino, P.M. *Clin. Cancer Res.* **15,** 3927-3937 (2009).
14. Handy, D.E., Castro, R., and Loscalzo, J. *Circulation* **123,** 2145-2156 (2011).

## Histone Acetylation, Deacetylation, and Genomic Bistability
**page 16**

1. Ptashne, M. *FASEB J.* **27(1),** 1-2 (2013).
2. Walsh, C.A., Qin, L., Tien, J.C.Y., *et al. Int. J. Biol. Sci.* **8(4),** 470-485 (2012).
3. Martin, D.G.E., Grimes, D.E., Baetz, K., *et al. Mol. Cell Biol.* **26(8),** 3018-3028 (2006).
4. Katan-Khaykovich, Y. and Struhl, K. *Genes Dev.* **16,** 743-752 (2002).
5. Dodd, I.B., Micheelsen, M.A., Sneppen, K., *et al. Cell* **129,** 813-822 (2007).
6. Danzer, J.R. and Wallrath, L.L. *Development* **131(15),** 3571-3580 (2004).
7. Johnson, A., Li, G., Sikorski, T.W., *et al. Mol. Cell* **35(6),** 769-781 (2009).
8. Margueron, R., Justin, N., Ohno, K., *et al. Nature* **461,** 762-767 (2009).
9. Wysocka, J., Swigut, T., Milne, T.A., *et al. Cell* **121,** 859-872 (2013).
10. Lai, K., Robertson, M.J., and Schaffer, D.V. *Biophys. J.* **86(5),** 2748-2757 (2004).
11. Lopes, F.J.P., Vieira, F.M.C., Holloway, D.M., *et al. PLoS Comput. Biol.* **4(9),** (2008).
12. Sneppen, K. and Dodd, I.B. *PLoS Comput. Biol.* **8(8),** (2012).

## Bromodomains, ChromoHub, & STRING
**page 26**

1. Filippakopoulos, P., Picaud, S., Mangos, M., *et al. Cell* **149(1),** 214-231 (2012).
2. Denis, G.V. *Discov. Med.* **10(55)**, 489-499 (2010).
3. Belkina, A.C. and Denis, G.V. *Nat. Rev. Cancer* **12,** 465-477 (2012).
4. Cliffe, S.T., Bloch, D.B., Suryani, S., *et al. J. Allergy Clin. Immunol.* **130(3),** 735-742 (2012).
5. Field, M., Tarpey, P.S., Smith, R., *et al. Am. J. Hum. Genet.* **81(2),** 367-374 (2007).
6. Bueno, C., Montes,R., Catalina, P., *et al. Leukemia* **25,** 400-410 (2011).
7. Tamkun,J.W., Deuring, R., Scott,M.P., *et al. Cell* **68,** 561-572 (1992).
8. Zippo, A., Serafini, R., Rocchigiani, M., *et al. Cell* **138,** 1122-1136 (2009).
9. Liu, L., Zhen, X.T., Denton, E., *et al. Bioinformatics* **28(16),** 2205-2206 (2012).
10. Szklarczyk, D., Franceschini, A., Kuhn, M., *et al. Nucleic Acids Res.* **39,** D561-D568 (2011).

## Histone Methylation and the Language of Epigenetics
**page 48**

1. de Groote, M.L., Verschure, P.J., and Rots, M.G. *Nucleic Acids Res.* **40(21),**
2. Janzen, W.P., Wigle, T.J., Jin, J., *et al. Drug Discov. Today Technol.* **7(1),** e59-e65 (2010).
3. Baker, L.A., Allis, C.D., and Wang, G.G. *Mutat. Res.* **647(1-2),** 3-12 (2008).
4. Maurer-Stroh, S., Dickens, N.J., Hughes-Davies, L., *et al. Trends Biochem. Sci.* **28(2),** 69-74 (2003).
5. Migliori, V., Mapelli, M., and Guccione, E. *Epigenetics* **7(8),** 815-822 (2012).
6. Dastidar, E.G., Dzeyk, K., Krijgsveld, J., *et al. PLoS One* **8(1),** (2013).
7. Katan-Khaykovich, Y. and Struhl, K. *Genes Dev.* **16,** 743-752 (2002).
8. Klose, R.J. and Zhang, Y. *Nat. Rev. Mol. Cell Biol.* **8(4),** 307-318 (2007).
9. Musselman,C.A., Lalonde, M.E., Côté, J., *et al. Nat. Struct. Mol. Biol.***19,** 1218-1227 (2012).

## Histone Demethylation
**page 58**

1. Bannister, A.J. and Kouzarides, T. *Cell Res.* **21,** 381-395 (2011).
2. Bannister, A.J., Schneider, R., and Kouzarides, T. *Cell* **109,** 801-806 (2002).
3. Shi, Y., Lan, F., Matson, C., *et al. Cell* **119,** 941-953 (2004).
4. Hakimi, M.-A., Bochar, D.A., Chenoweth, J., *et al. Proc. Natl. Acad. Sci. USA* **99(11),** 7420-7425 (2002).
5. Metzger, E., Wissmann, M., Yin, N., *et al. Nature* **437,** 436-439 (2005).
6. Ciccone, D.N., Su, H., Hevi, S., *et al. Nature* **461,** 415-418 (2009).
7. Tsukada, Y., Fang, J., Erdjument-Bromage, H., *et al. Nature* **439(16),** 811-816 (2006).
8. Webby, C.J., Wolf, A., Gromak, N., *et al. Science* **325,** 90-93 (2009).
9. Del Rizzo, P.A., Krishnan, S., and Trievel, R.C. *Mol. Cell Biol.* **32(19),** 4044-4052 (2012).
10. Krishnan, S., Collazo, E., Ortiz-Tello, P.A., *et al. Anal. Biochem.* **420,** 48-53 (2012).
11. Sekirnik, R., Rose, N.R., Mecinovic, J., *et al. Metallomics* **2(6),** 397-399 (2010).
12. Chase, A. and Cross, N.C.P. *Clin. Cancer Res.* **17(9),** 2613-2618 (2011).
13. Grasso, C.S., Wu, Y.-M., Robinson, D.R., *et al. Nature* **487,** 239-243 (2012).
14. Kruidenier, L., Chung, C.-W., Cheng, Z., *et al. Nature* **488,** 404-408 (2012).

# Alphabetical Index

# I



# J



# K



# L



# M



# N



# O





# P



# Q

# R



# S

## T



## U



## V



## W



## X



## Y

## Z





# Item No. Index


vol. 18
Ep
Epigenetics &
Gene Regulation
(800) 364 9897
www.caymanchem.com