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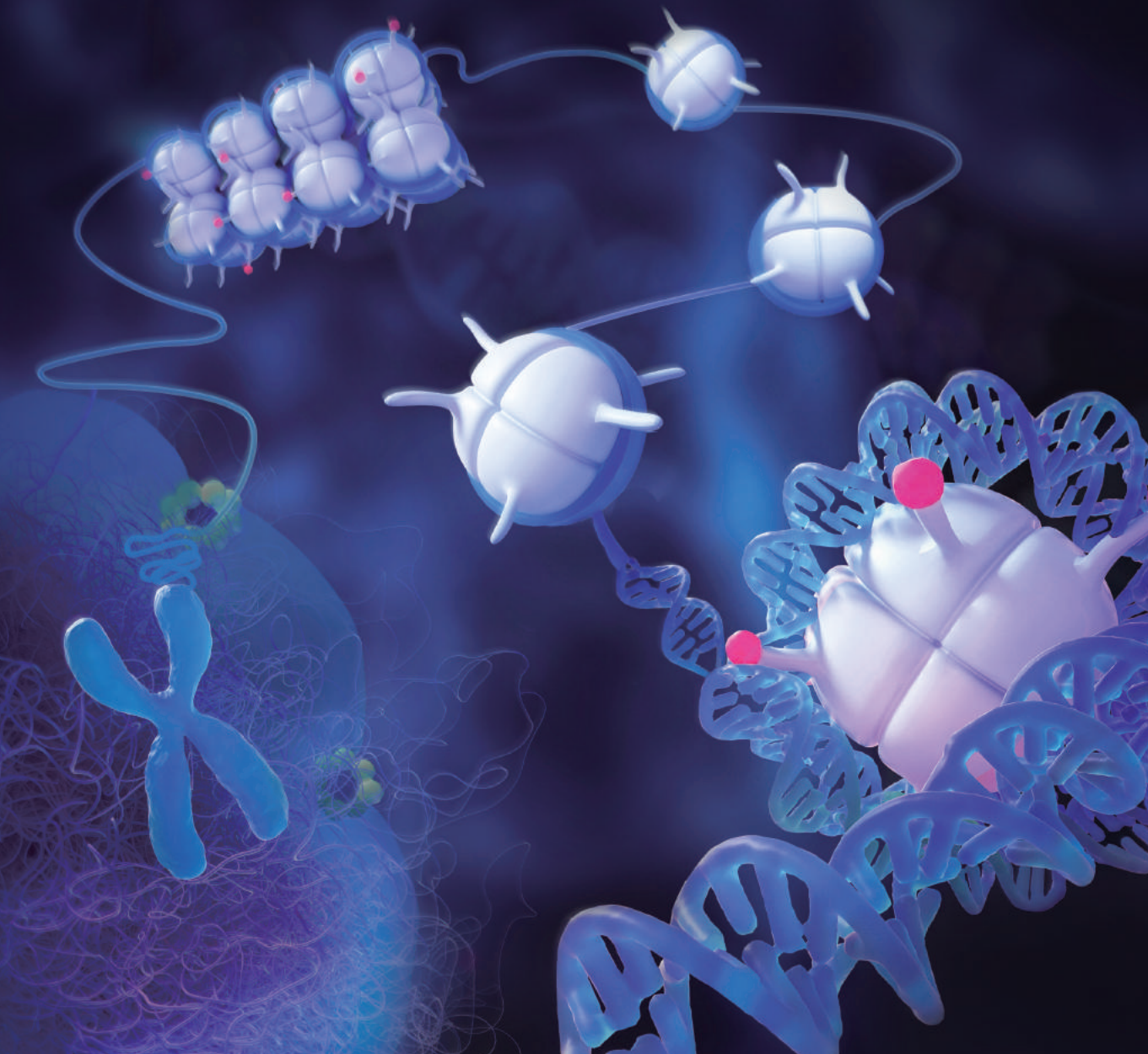
Epigenetics
Product Handbook



Epigenetics

Epigenetic mechanisms include any process that alters gene function without changing the DNA sequence and are mitotically and/or meiotically heritable. Many types of epigenetic processes have been identified, including DNA methylation, alterations in the structure of histone proteins, and gene regulation by small non-coding RNAs.

Disruption of gene expression patterns controlled by epigenetics can lead to autoimmune diseases, cancer, and a variety of other diseases. Enzymes such as HDACs and DNMTs involved in epigenetic inheritance serve as epigenetic targets with numerous inhibitors already approved by the FDA, and many are undergoing clinical trials for the same purpose. Drugs that inhibit DNA methylation or histone deacetylation (such as **5-azacitidine**, **Decitabine**, and **Vorinostat**) have been studied for the reactivation of tumor suppressor genes and repression of cancer cell growth[1]. The development of epigenetic drugs is emerging as a promising way to treat these diseases[1].

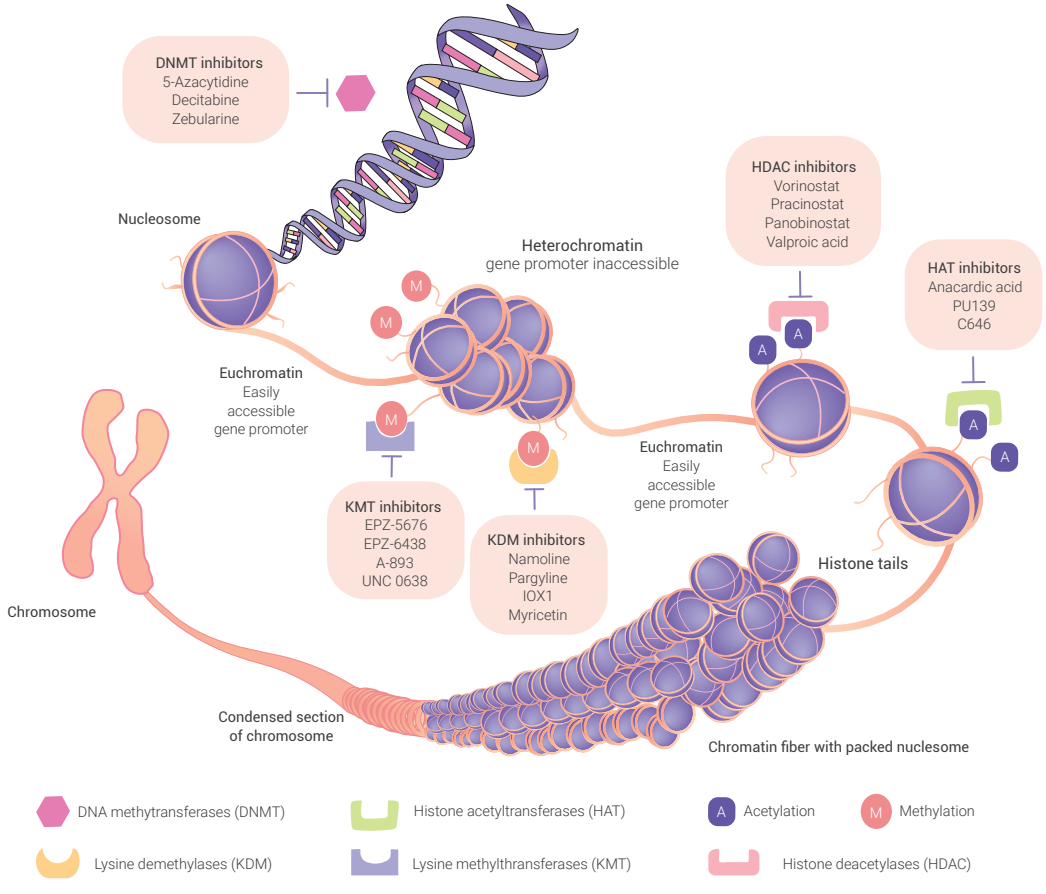


Figure 1. Epigenetic targets[2].

CONTENTS

Histone Modifications

Histone modifications are able to alter chromatin structure and are associated with both transcriptional activation and inhibition. Histone modifications can either activate or silence gene expression, depending on the residues added to the targeted histones and the extent of the modification. There are various kinds of histone modifications, including **acetylation, methylation, citrullination, deamination, ubiquitination**, and **ADP-ribosylation**.

Histone acetylation usually occurs on basic amino acids such as lysine and arginine. In general, acetylation activates gene expression by reducing the affinity of histones to DNA. Histone acetylation is transfered by HATs and removed by HDACs. HATs can be grouped into at least five subfamilies, including **GNAT, MYST, p300/CBP, the general transcription factor HATs**, and **the nuclear hormone-related HATs**. CBP/p300 contains a bromodomain that is important in binding to chromatin, and has attracted widespread attention as promising epigenetic targets for diverse human diseases[3].

Methylation, another widely studied histone modification, is catalyzed by histone methyltransferases. Histone methylation can either activate or silence gene expression. For example, H3K4me3 activates gene expression, while H3K27me3 is associated with gene silencing. Histone demethylation is performed by two classes of histone demethylases: lysine-specific demethylase (LSD) family proteins (LSD1 and LSD2) and JmjC domain-containing histone demethylase (JHDM)[4].

Other histone modifications are relatively rare, including histone deamination/citrullination, ubiquitination, ADP-ribosylation, N6-formylation, and O-GlcNAylation. For example, ADP-ribosylation of lysine residues occurs in less than 1% of histone proteins, but is observed particularly in the case of single DNA strand breaks[5].

Enzymes that mediate histone modification marks (such as HATs) are known as "writers", while enzymes that remove these modifications are called "erasers". In addition, some protein with domains have also been identified that can recognize specific histone modifications (i.e., readers). For example, the bromodomains of BET proteins selectively target acetyllysine residues, whereas JMJD2A and 53BP1 with tudor domains bind methylated arginines[6].

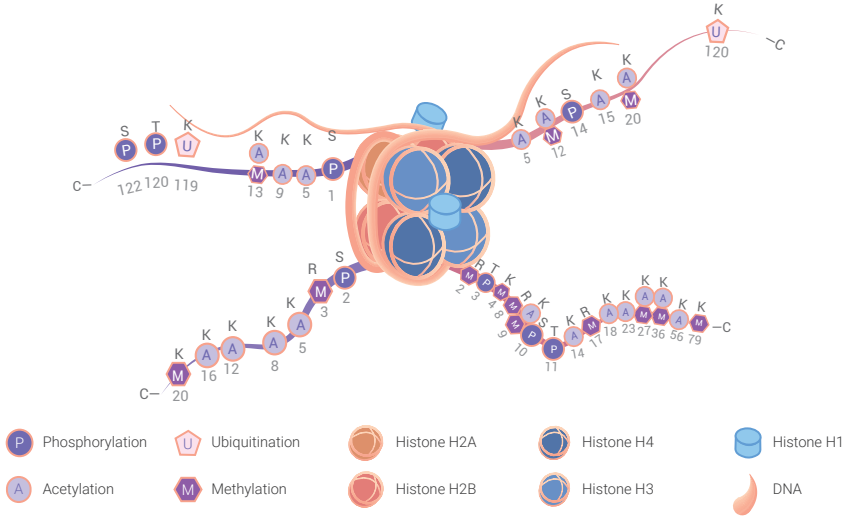


Figure 2. Histone modifications[2].

MCE provide 1,000+ histone modifications related products, covering hot targets including HDACs, HATs, histone demethylase, histone methyltransferase, PARP, BET proteins and others.

Compounds			
Cat. No.	**Product Name**	**Description**	**Type**
HY-100201	A-196	A selective inhibitor of SUV420H1 and SUV420H2, for the research of the role of histone methyltransferases in genomic integrity.	Methylation
HY-101451	PBIT	A specific inhibitor of the JARID1 enzymes.	Methylation
HY-102047B	KDOAM-25 citrate	A highly selective KDM5 inhibitor, increases global H3K4 methylation at transcriptional start sites.	Methylation
HY-10587	BIX-01294	A reversible and highly selective G9a and GLP Histone Methyltransferase inhibitor	Methylation
HY-112445	SGC3027	A histone methyltransferase inhibitor, the first selective and cell active chemical probe for PRMT7.	Methylation
HY-114208A	BI-9321 trihydrochloride	A selective and cellular active nuclear receptor-binding SET domain 3 (NSD3)-PWWP1 domain antagonist.	Methylation
HY-120137	CMP-5	A selective PRMT5 inhibitor, prevents EBV-driven B-lymphocyte transformation but leaves normal B cells unaffected.	Methylation
HY-12583	A-366	A highly selective, peptide-competitive histone methyltransferase G9a inhibitor, and an inhibitor of the Spindlin1-H3K4me3-interaction.	Methylation
HY-13643	Daminozide	A plant growth regulator and KDM2/7 histone demethylases inhibitor.	Methylation
HY-13807	UNC0646	A selective histone methyltransferase G9a and GLP inhibitor.	Methylation
HY-13808	UNC 0631	A potent histone methyltransferase G9a inhibitor.	Methylation
HY-15223	MI-3	A potent and high affinity menin-MLL inhibitor.	Methylation
HY-15650	SGC0946	A selective DOT1LH3K79 methyltransferase inhibitor.	Methylation
HY-W015114	L-2-Hydroxyglutaric acid disodium	Inhibits histone demethylases and hence promotes histone methylation, used in the research of renal cancer.	Methylation
HY-100508	ITSA-1	A HDAC activator, counteracts Trichostatin A (TSA)-induced cell cycle arrest, histone acetylation, and transcriptional activation.	Acetylation
HY-100719	BRD-6929	A selective brain-penetrant inhibitor of HDAC1 and HDAC2, used for mood-related behavioral model research.	Acetylation
HY-101084	NSC 228155	An EGFR activator and an inhibitor of KIX-KID interaction, inhibits KID from CREB and KID-interacting domain (KIX) from CBP.	Acetylation

Compounds			
Cat. No.	**Product Name**	**Description**	**Type**
HY-107569	Garcinol	A histone acetyltransferases (HATs) and p300/CPB-associated factor inhibitor, has anti-inflammatory and anti-cancer activity.	Acetylation
HY-112789	(+)-JQ1 PA	A BET inhibitor, with an IC_{50} of 10.4 nM.	Acetylation
HY-128359	ACBI1	A cooperative SMARCA2, SMARCA4 and PBRM1 PROTAC degrader, induces apoptosis.	Acetylation
HY-128918	SIS17	A speific mammalian histone deacetylase 11 (HDAC 11) inhibitor.	Acetylation
HY-13216	Pyroxamide	A HDAC1 inhibitor, induces apoptosis and cell cycle arrest.	Acetylation
HY-15144	Trichostatin A	A potent and specific inhibitor of HDAC class I/II.	Acetylation
HY-15149	Romidepsin	Inhibits HDAC1, HDAC2, HDAC4, and HDAC6, induces cell G2/M phase arrest and apoptosis.	Acetylation
HY-15489	Scriptaid	A HDAC inhibitor, a sensitizer to antivirals and has potential for EBV-associated lymphomas research.	Acetylation
HY-15654	Sodium 4-phenylbutyrate	An inhibitor of HDAC and endoplasmic reticulum (ER) stress, used in cancer and infection research.	Acetylation
HY-15658	GSK2801	A selective, orally active and cell active acetyl-lysine competitive BAZ2A and BAZ2B bromodomains inhibitor.	Acetylation
HY-15815	Bromosporine	A BET inhibitor, arrests cell cycle and induces apoptosis in cancer cells.	Acetylation
HY-15846	CPI-203	A potent and selective inhibitor of BET bromodomain.	Acetylation
HY-16586	PFI-1	A selective BET inhibitor for BRD4.	Acetylation
HY-19999A	PF-CBP1 hydrochloride	A highly selective inhibitor of the CREB binding protein bromodomain (CBP BRD), used for the research of neurological disorders.	Acetylation
HY-A0281	4-Phenylbutyric acid	An inhibitor of HDAC and endoplasmic reticulum (ER) stress, used in cancer and infection research.	Acetylation
HY-N0005	Curcumin	A natural phenolic compound, is a p300/CREB-binding protein-specific inhibitor of acetyltransferase.	Acetylation
HY-N6735	Apicidin	A fungal metabolite, acts as a HDAC inhibitor, with antiparasitic activity and a broad spectrum antiproliferative activity.	Acetylation
HY-W013274	CPTH2	A HAT inhibitor, inhibits the histone H3 acetylation by Gcn5, decreases the invasiveness of a ccRCC cell line through the inhibition of KAT3B.	Acetylation

Compound Screening Libraries

Cat. No. : HY-L005

Epigenetics Compound Library

A unique collection of **1,000+** epigenetics-related compounds.
Main targets: HDAC, Histone Demethylase, Histone Acetyltransferase (HAT), DNA Methyltransferase (DNMT), Epigenetic Reader Domain, MicroRNA, etc.

Cat. No. : HY-L024

Histone Modification Research Compound Library

A unique collection of **500+** bioactive compounds targeting Epigenetic Reader Domain.
Main targets: HDAC, Histone Acetyltransferase, Sirtuin, Histone Demethylase, Histone Methyltransferase, etc.

Proteins, Peptides & Inhibitor Cocktail

Cat. No.	Product Name	Description	Type
HY-P72336	**Human/Xenopus laevis Histone H4**	One of the five main histone proteins involved in the structure of chromatin in eukaryotic cells.	Proteins
HY-P76080	**Human SMYD3**	A member of the lysine methyltransferase family, plays an important role in the methylation of histone/non-histone targets.	Proteins
HY-P72262	**Human Histone deacetylase 1**	HDACs play important roles in the regulation of gene expression, apoptosis, stress responses, DNA repair, genomic stability.	Proteins
HY-P71592	**Mouse Sap130**	May function in the assembly and/or enzymatic activity of mSin3A or in mediating interactions between the complex and other regulatory complexes.	Proteins
HY-P75551	**Human LSD1**	Demethylates mono- and dimethyl-lysine on histone H3 to control chromatin structure, resulting in transcriptional regulation.	Proteins
HY-P2509	**Histone H2A (1-20)**	A 35-residue a peptide of histone H2A, is a substrate for methyltransferase/demethylase enzymes.	Peptides
HY-P2258	**Histone H3 (1-34)**	A peptide derived from human histone isotype 3.1. Histone variants and histone modifications modulate chromatin structure, ensuring the precise operation of cellular processes associated with genomic DNA.	Peptides
HY-P2257	**H3K4 (Me3) (1-20)**	A histone peptide. Trimethylation of H3K4 me3 is found in active euchromatin but not in silent heterochromatin.	Peptides
HY-P2480	**Histone H1-derived Peptide**	A phosphopeptide and the peptide substrates contains a sequence in accordance with the optimal recognition motif for CDKs.	Peptides

Cat. No.	Product Name	Description	Type
HY-K0030	Deacetylase Inhibitor Cocktail (100X)	Deacetylase Inhibitor Cocktail is a synergistic combination of chemicals designed to preserve the acetylation state of proteins.	Inhibitor Cocktail
HY-K0011	Protease Inhibitor Cocktail, mini-Tablet	Protease inhibitor cocktail is used in cell lysates or tissue extracts to increase protein stability.	Inhibitor Cocktail
HY-K0013	Protease and Phosphatase Inhibitor Cocktail (EDTA-Free, 10× in ddH_2O)	Protease and Phosphatase Inhibitor Cocktail (EDTA-Free, 10× in ddH_2O) protects protein from degradation by endogenous proteases released during protein extraction and purification.	Inhibitor Cocktail

DNA Methylation

DNA methylation is a common epigenetic alteration and considered a heterochromatin mark. DNA methylation plays an important role in maintaining the stability of genome, genomic imprinting, X-chromosome inactivation in females, regulation of transcription, and also in the developmental process of an organism[2].

DNA methylation modifications include 5-methylcytosine (5mC), N6-methylladenine (6mA) and 4-methylcytosine (4mC). Among them, 6mA and 4mC are prevalent in prokaryotic genomes, 5mC is the most widely distributed type of methylation in eukaryotes. DNA methyltransferases (DNMTs) target CpG sites and actively methylate DNA. DNMT3A/B are the "de novo" DNMTs and transfer methyl groups onto naked DNA (Figure 3a). However DNMT1 preserves preexisting pattern of methylation after cell replication (Figure 3b)[4][7]. DNA methylation is recognized by three separate families of proteins: the MBD (methyl-CpG-binding domain) proteins, the UHRF (ubiquitin-like, containing PHD and RING finger domain) proteins, and the zinc-finger proteins[7].

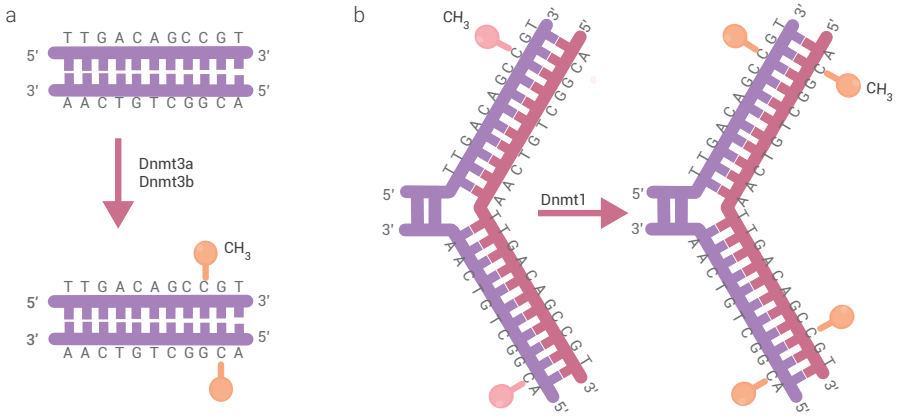


Figure 3. DNA methylation pathways[3].

DNA demethylation is characterized as either passive or active. The inhibition or dysfunction of DNMTs allows newly incorporated cytosine to remain unmethylated and consequently reduces the overall methylation level following each cell division. Active DNA demethylation requires enzymes such as activation-induced cytidine deaminase (AID) and ten-eleven translocation (TET) enzymes to process 5mC in order to revert it back to a naked cytosine[4].

MCE offers 100+ compounds related to DNA methylation, covering various targets including DNMTs, TET enzymes, cytidine deaminase, UHRF proteins, MBD proteins, EZH2, and others.

Compounds			
Cat. No.	**Product Name**	**Description**	**Type**
HY-101925	CM-272	A selective and reversible dual G9a/DNA methyltransferases (DNMTs) inhibitor with antitumor activities.	Methylation
HY-103236	NSC232003	A highly potent UHRF1 inhibitor, which inhibits DNA methylation in vitro and disrupts DNMT1/UHRF1 interactions.	Methylation
HY-103397	Nanaomycin A	A quinone antibiotic and the first selective DNMT3B inhibitor, with anti-tumor and anti-parasite activity.	Methylation
HY-10586	5-Azacytidine	A nucleoside analogue of cytidine that specifically inhibits DNA methylation, induces cell autophagy.	Methylation
HY-116217	5-Fluoro-2'-deoxycytidine	A tumor-selective prodrug of the potent thymidylate synthase inhibitor 5-fluoro-2'-dUMP (a DNMT inhibitor).	Methylation
HY-125292	NV03	A selective antagonist of UHRF1- H3K9me3 interaction by binding to UHRF1 tandem tudor domain.	Methylation
HY-12746	DC-05	A DNA methyltransferase 1 (DNMT1) inhibitor.	Methylation
HY-12747	DC_517	A DNA methyltransferase 1 (DNMT1) inhibitor.	Methylation
HY-13057	O6BTG-octylglucoside	A potent O^6-methylguanine-DNAmethyl-transferase (MGMT) inhibitor.	Methylation
HY-13420	Zebularine	A DNA methyltransferase inhibitor, inhibits cytidine deaminase.	Methylation
HY-13642	RG108	A non-nucleoside DNA methyltransferases (DNMTs) inhibitor, causes demethylation and reactivation of tumor suppressor genes.	Methylation
HY-13668	Lomeguatrib	A potent O^6-methylguanine-DNAmethyl-transferase (MGMT) inhibitor.	Methylation
HY-13962	SGI-1027	A DNA methyltransferase (DNMT) inhibitor, induces apoptosis.	Methylation
HY-103236	NSC232003	A potent UHRF1 inhibitor, inhibits DNA methylation *in vitro* and disrupts DNMT1/UHRF1 interactions.	Methylation
HY-131031	KCC-07	A selective and brain-penetrant MBD2 (methyl-CpG-binding domain protein 2) inhibitor, prevents binding of MBD2 to methylated DNA.	Methylation
HY-144904	MC4343	A potent and dual inhibitor of EZH2 and HDAC.	Methylation

Compounds			
Cat. No.	Product Name	Description	Type
HY-A0004	Decitabine	An orally active deoxycytidine analogue antimetabolite and a DNA methyltransferase inhibitor, with anti-cancer activity.	Methylation
HY-B2194	γ-Oryzanol	Significantly inhibits the activities of DNMT1, DNMT3a.	Methylation
HY-B2230	Hinokitiol	Reduces Nrf2 expression, decreases DNMT1 and UHRF1 mRNA and protein expression, with anti-infective, and anti-tumor activities.	Methylation
HY-129079A	TFMB-(S)-2-HG	A potent inhibitor of the 5'-methylcytosine hydroxylase TET2, also inhibits the EglN prolyl hydroxylases.	Demethylation
HY-113038B	α-Hydroxyglutaric acid	Inhibits multiple α-ketoglutarate-dependent dioxygenases, including histone demethylases and the TET family of 5mC hydroxylases.	Demethylation
HY-15345	Tetrahydrouridine dihydrate	A potent inhibitor of cytidine deaminase (CDA).	Demethylation
HY-120395	UC-514321	Directly targets STAT3/5 and represses TET1 expression.	Demethylation

Small non-coding RNAs (ncRNAs)

In the 1990s, it was found that small double-stranded RNAs (dsRNAs) were able to mediate post-transcriptional gene silencing of complementary mRNAs in the nematode *Caenorhabditis elegans* through a process called **RNA interference (RNAi)**. This discovery led to the realization that small ncRNAs are key regulators of gene expression in many different cellular pathways and systems. MicroRNAs (miRNAs) and endogenous small interfering RNAs (siRNAs) are the most thoroughly investigated non-coding RNAs[8].

SiRNA is a small exogenous dsRNA (~20 nts), which triggers the RNAi pathway. It unwinds and the sense strand is degraded. The antisense strand forms an RNA-induced silencing complex (RISC) with various protein components. The antisense strand retained in RISC is specifically complementary to the target gene mRNA. Meanwhile, RISC can cut and degrade the target mRNA, inhibiting the target gene expression. Incomplete complementarity results in mRNA translation inhibition[9].

MiRNAs are highly evolutionarily conserved and small single-stranded ncRNAs (~22 nts). The primary mode of action for miRNA and siRNA is similar; both form RISC complexes that trigger endogenous RNAi by regulating the stability or inducing mRNA degradation. However, miRNAs usually bind to the 3'-UTR of mRNA. For mammals, the base pairing is always imperfect, resulting in suppression of mRNA translation[10]. Meanwhile, plant miRNAs bind with near-perfect complementarity to sites within the coding sequence of their targets, and the mRNA of target genes is sliced and degraded[11].

Currently, the utilization of small ncRNAs as drugs has become a relatively novel approach compared to conventional small molecule inhibitors. The recent FDA approvals of **Givosiran**, **Lumasiran**, and **Viltolarsen** have ushered in the wave of RNAi or RNA-based therapies into the mainstream of drug development. The potential of RNA therapies in precision genetics has raised enthusiasm for similar applications in cancer, cardiovascular diseases, and rare disease therapies[12].

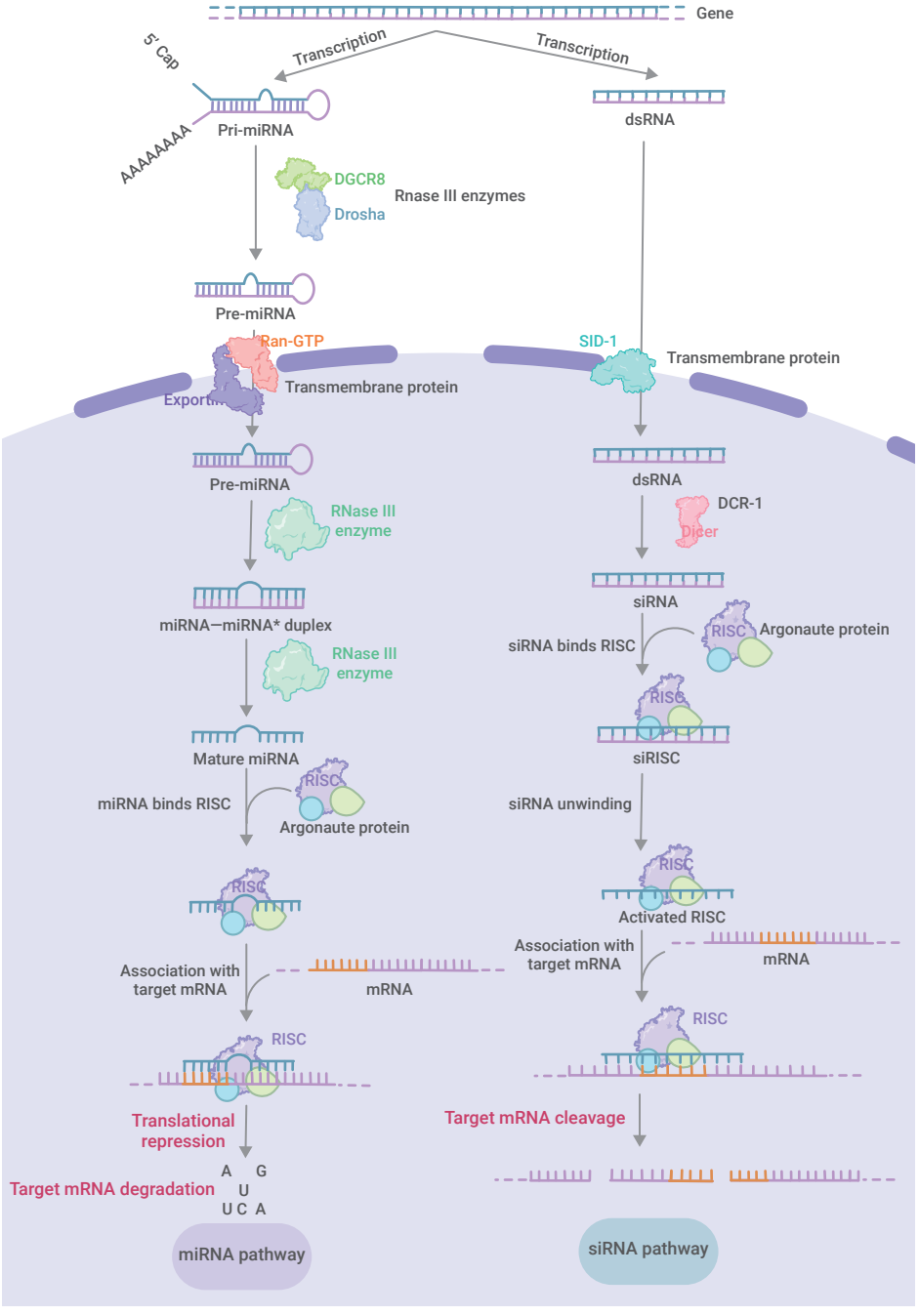


Figure 4. Formation mode and regulatory mechanisms of miRNA and siRNA[9].

MCE offers **4,000+** compounds related to Non-coding RNAs, including miRNAs, siRNAs, liposome for siRNA delivery, antisense oligonucleotide (ASO), and others.

Compounds			
Cat. No.	**Product Name**	**Description**	**Type**
HY-132588	Lumasiran	Inhibits the synthesis of oxalate, which is the toxic metabolite that is directly associated with the clinical manifestations of PH1.	siRNA
HY-132591	Inclisiran	Inhibits PCSK-9 transcription, for cardiovascular disease research.	siRNA
HY-132596	Tivanisiran	A siRNA was designed to silence TRPV1, used for the study of dry eye disease.	siRNA
HY-132610	Givosiran	A siRNA that targets hepatic ALAS1 messenger RNA, used for the research of acute intermittent porphyria.	siRNA
HY-108753	Eteplirsen	Targets exon 51 in defective gene variants, used for Duchenne muscular dystrophy research.	ASO
HY-112980	Nusinersen	Modifies pre-messenger RNA splicing of the SMN2 gene and thus promotes increased production of full-length SMN protein.	ASO
HY-132586	Viltolarsen	Targets the splicing of exon 53 in the dystrophin gene, used for the research of the Duchenne muscular dystrophy (DMD).	ASO
HY-132600	RG-101	Antagonizes miR-122. miR-122 is an important host factor for hepatitis C virus (HCV) replication.	ASO
HY-132608	Inotersen sodium	Targets the TTR transcript and reduces the TTR mRNA levels, for the research of hereditary TTR amyloidosis polyneuropathy.	ASO
HY-132611	Golodirsen	Specifically targets exon 53 of dystrophin pre-mRNA, used for the research of Duchenne muscular dystrophy (DMD).	ASO
HY-139290	RGLS4326	A first-in-class, short oligonucleotide miR-17 inhibitor, for the research of autosomal dominant polycystic kidney disease (ADPKD).	ASO
HY-143230	Custirsen	A clusterin inhibitor, an antiapoptotic protein that is upregulated in response to chemotherapy and that confers treatment resistance.	ASO
HY-145729	Danvantisen	An antisense oligonucleotide for STAT3 with antitumor activity.	ASO
HY-150724	ODN 1018	A TLR-9 agonist, used as a vaccine adjuvant.	CpG ODN
HY-150741	ODN 2216	A TLR-9 agonist, induces IFN-α/IFN-β, used as a vaccine adjuvant.	CpG ODN
HY-135276	Targaprimir-96	Inhibits miR-96 processing, selectively modulates miR-96 production in cancer cells and triggers apoptosis.	Small Molecule

Compounds

Cat. No.	Product Name	Description	Type
HY-15861	Targapremir-210	A selective miR-210 inhibitor. Targapremir-210 inhibits pre-miR-210 processing with high binding affinity.	Small Molecule
HY-112005	DOPE	A neutral helper lipid for cationic liposome, improves transfection efficiency of naked siRNA.	Lipid
HY-112251	D-Lin-MC3-DMA	An ionizable cationic lipid, is a potent siRNA delivery vehicle.	Lipid
HY-130751	DODAP	A cationic lipid, used to encapsulate siRNA.	Lipid
HY-134541	SM-102	An ionizable amino lipid, used for the formation of LNPs.	Lipid
HY-145795	OF-02	An alkenyl amino alcohol (AAA) ionizable lipid for highly potent in vivo mRNA delivery.	Lipid
HY-N0322	Cholesterol	The major sterol in mammals, makes up 20-25% of structural components of the plasma membrane.	Lipid
HY-W040193	DSPC	A cylindrical-shaped lipid, used to synthesize liposomes, and is the lipid component in the lipid nanoparticle (LNP) system.	Lipid
HY-138300	ALC-0159	A polyethylene glycol (PEG) lipid conjugate, could be used as vaccine excipient.	Lipid

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MedChemExpress USA

Tel: 609-228-6898 **E-mail:** sales@MedChemExpress.com
Fax: 609-228-5909 **Tech Support:** tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA

MedChemExpress Europe

Tel: + 46 86500910 **E-mail:** eu.sales@MedChemExpress.com
Address: Bergkällavägen 37C, 192 79 Sollentuna, SWEDEN