

EPIGENETIC & DNA-RELATED ENZYMES

Epigenetics describes a stably heritable change in phenotype or gene expression in an organism or cell, resulting from changes in a chromosome that is not caused by a change in DNA sequence. The epigenetic regulation of gene transcription is a key biological determinant of cellular differentiation. There are three distinct classes of epigenetic information that can be stably inherited over cell divisions: DNA methylation, non coding RNAs, and histone modifications. DNA methylation is the best understood and the most extensively studied epigenetic mechanism. Histone modification includes acetylation/deacetylation, phosphorylation, ubiquitination and methylation/demethylation.

Cerep has developed a large panel of histone deacetylases (HDAC). HDACs remove the acetyl groups from the lysine residues leading to the formation of a condensed and transcriptionally silenced chromatin. HDAC inhibitors block this action, thereby affecting gene expression. Different DNA methylase enzymes are under development and will be available soon.

Classical genetic includes the DNA replication and DNA repair enzymes. Both families of enzyme are involved in mitosis and ensure that exact copies of the DNA in chromosomes are passed on to daughter cells. To carry out gene expression, and to replicate chromosomes, a cell must control the coiling and uncoiling of DNA, around DNA itself and around histones. This is accomplished with different types of enzymes such as topoisomerases. Topoisomerases are critical for maintaining normal DNA topography and Topoisomerase inhibitors cause breaks in the DNA strand leading to cell death.

Different classes of epigenetic enzymes have been demonstrated to have strong disease association and are currently being targeted for small molecule inhibition in cancer therapy. Mutation in genes critical to cellular growth and survival can also cause and promote cancer. Another class of enzymes called kinesins, are also interesting as anticancer agents, as they are present in actively dividing cells only during mitosis. Cerep has developed Eg5 and CENPE which help chromosomes align and separate during mitosis.


The assays below allow elucidation of compounds activity on a number of enzymes involved in epigenetics and DNA function. Extensive research is aimed at discovering small molecule inhibitors against them for therapeutic use.

→ The list below includes all epigenetic and DNA-related enzymes available at March 1st, 2011.
Cerep will focus part of its R&D effort in 2011 to develop new assays in this field.
For further information, please contact us at: sales@cerep.com

DNA REPAIR & MITOTIC ENZYMES

CENPE

Ref. **2150**

 3 weeks

Included in:

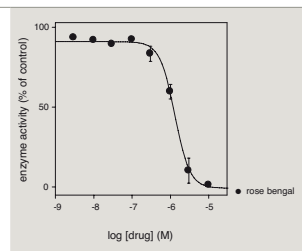
- ▶ Non-kinase enzyme profile
- ▶ Diversity profile
- ▶ Organ safety profile

Source  human recombinant (*E. coli*)

Substrate ATP (100 μ M)
Measured product inorganic phosphate
Detection method photometry

Reference rose bengal (IC₅₀: 1.3 μ M)

Goldstein, L.S.B. (1993) *An. Rev. Genetic*, **27**: 319-351.



DNA polymerase α

Ref. **2348**

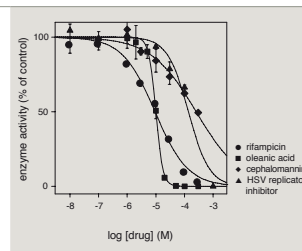
 6 weeks

Source bacterial recombinant (*E. coli*)

Substrate [³H]TTP (300 nM)
Measured product [³H]TTP incorporation
Detection method scintillation counting

Reference rifampicin (IC₅₀: 9.3 μ M)

Tuske, S. et al. (2000) *J. Biol. Chem.*, **275**: 23759-23768.



DNA polymerase β

Ref. **2445**

 3 weeks

Included in:

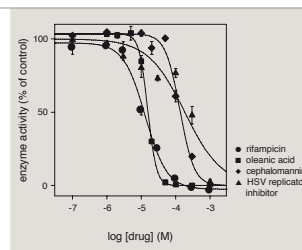
- ▶ Organ safety profile

Source  human recombinant (*E. coli*)

Substrate [³H]TTP (50 μ M)
Measured product [³H]TTP incorporation
Detection method scintillation counting

Reference rifampicin (IC₅₀: 12 μ M)

Tuske, S. et al. (2000) *J. Biol. Chem.*, **275**: 23759-23768.



Anticipating clinical effects from *in vitro* data

Eg5

Ref. **2151**

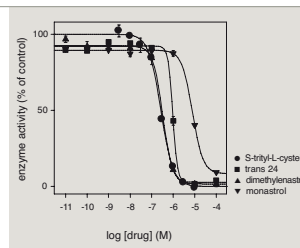
3 weeks

Included in:

- ▶ Non-kinase enzyme profile
- ▶ Diversity profile
- ▶ Organ safety profile

Source human recombinant
 Substrate ATP (50 μ M)
 Measured product inorganic phosphate
 Detection method photometry
 Reference S-trityl-L-cysteine (IC₅₀: 365 nM)

Goldstein, L.S.B. (1993) *An. Rev. Genetic*, **27**: 319-351.



topoisomerase II

Ref. **2430**

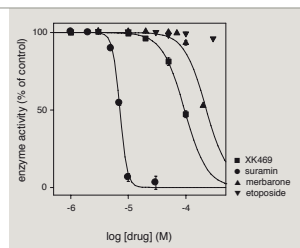
[CUSTOM OFFER]

Please contact us at:

customresearch@cerep.com

Source human recombinant
 Substrate supercoiled pN01 plasmid DNA substrate (25 μ g/mL)
 Measured product triplex formation (substrate/oligo-nucleotide)
 Detection method fluorimetry
 Reference XK469 (IC₅₀: 90 μ M)

Maxwell, A. et al. (2006) *Nucleic Acids Res.*, **34**: 1-7.



HDACs

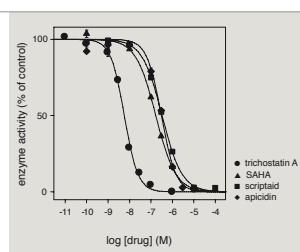
HDAC1

Ref. **2491**

3 weeks

Source human recombinant
 Substrate fluorogenic HDAC substrate (20 μ M)
 Measured product fluoro-lysine
 Detection method fluorimetry
 Reference trichostatin A (IC₅₀: 7.2 nM)

Strahl, B.D. and Allis, C.D. (2000) *Nature*, **403**: 41-45.



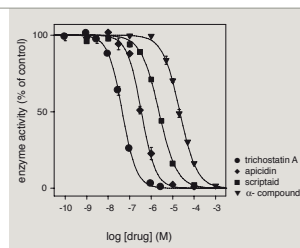
HDAC2

Ref. **2492**

3 weeks

Source human recombinant
 Substrate fluorogenic HDAC substrate (20 μ M)
 Measured product fluoro-lysine
 Detection method fluorimetry
 Reference trichostatin A (IC₅₀: 45 nM)

Strahl, B.D. and Allis, C.D. (2000) *Nature*, **403**: 41-45.



HDAC3

Ref. **2083**

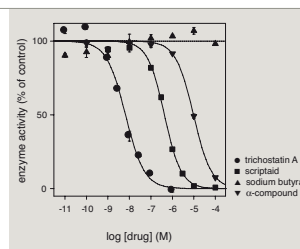
3 weeks

Included in:

- ▶ Non-kinase enzyme profile
- ▶ Diversity profile
- ▶ Organ safety profile

Source human recombinant
 Substrate fluorogenic HDAC substrate (50 μ M)
 Measured product fluoro-lysine
 Detection method fluorimetry
 Reference trichostatin A (IC₅₀: 5 nM)

Strahl, B.D. and Allis, C.D. (2000) *Nature*, **403**: 41-45.



HDAC4

Ref. **2493**

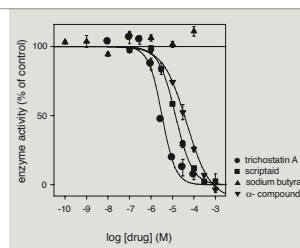
3 weeks

Included in:

- ▶ Non-kinase enzyme profile
- ▶ Diversity profile
- ▶ Organ safety profile

Source human recombinant
 Substrate fluorogenic HDAC substrate class 2a (20 μ M)
 Measured product fluoro-lysine
 Detection method fluorimetry
 Reference trichostatin A (IC₅₀: 3.3 μ M)


Strahl, B.D. and Allis, C.D. (2000) *Nature*, **403**: 41-45.



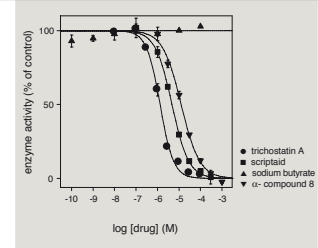
HDAC5

Ref. **2494**

🕒 3 weeks

Source  human recombinant
 Substrate fluorogenic HDAC substrate class 2a (20 µM)
 Measured product fluoro-lysine
 Detection method fluorimetry
 Reference trichostatin A (IC₅₀: 1.3 µM)

Strahl, B.D. and Allis, C.D. (2000) Nature, 403: 41-45.




HDAC6

Ref. **2495**

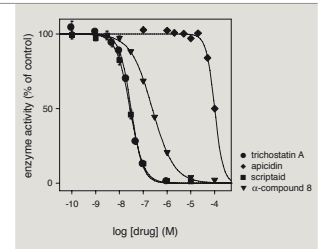
🕒 3 weeks

Included in:

- ▶ Non-kinase enzyme profile
- ▶ Diversity profile
- ▶ Organ safety profile

Source  human recombinant
 Substrate fluorogenic HDAC substrate (25 µM)
 Measured product fluoro-lysine
 Detection method fluorimetry
 Reference trichostatin A (IC₅₀: 30 nM)


Strahl, B.D. and Allis, C.D. (2000) Nature, 403: 41-45.



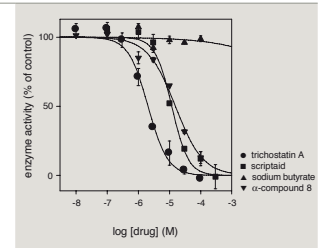
HDAC7

Ref. **2610**

🕒 3 weeks

Source  human recombinant
 Substrate fluorogenic HDAC substrate class 2a (50 µM)
 Measured product fluoro-lysine
 Detection method fluorimetry
 Reference trichostatin A (IC₅₀: 2.1 µM)


Strahl, B.D. and Allis, C.D. (2000) Nature, 403: 41-45.



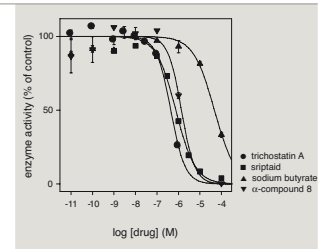
HDAC8

Ref. **2247**

🕒 3 weeks

Source  human recombinant
 Substrate fluorogenic HDAC substrate (400 µM)
 Measured product fluoro-lysine
 Detection method fluorimetry
 Reference trichostatin A (IC₅₀: 400 nM)


Strahl, B.D. and Allis, C.D. (2000) Nature, 403: 41-45.



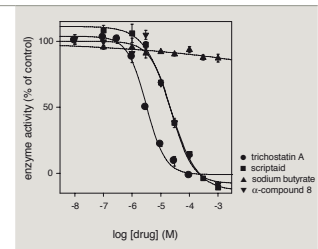
HDAC9

Ref. **2611**

🕒 3 weeks

Source  human recombinant
 Substrate fluorogenic HDAC substrate class 2a (50 µM)
 Measured product fluoro-lysine
 Detection method fluorimetry
 Reference trichostatin A (IC₅₀: 3 µM)


Strahl, B.D. and Allis, C.D. (2000) Nature, 403: 41-45.



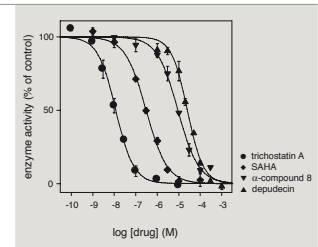
HDAC10

Ref. **2662**

🕒 3 weeks

Source  human recombinant
 Substrate fluorogenic HDAC substrate (20 µM)
 Measured product fluoro-lysine
 Detection method fluorimetry
 Reference trichostatin A (IC₅₀: 1.3 nM)

Strahl, B.D. and Allis, C.D. (2000) Nature, 403: 41-45.



FOR FURTHER DETAILS AND UPDATED INFORMATION ON ASSAYS:

■ Please go to www.cerep.com **CATALOG ONLINE** or contact us at sales@cerep.com

■ Europe: +33 (0)5 49 89 30 00 – USA: +1 (425) 895 8666 – Japan: +81 (0)3 3354 4026 – China: +86 21 5132 0568

🕒 Assay developed in 2010  New assay conditions  Human  Standard turnaround time


HDAC11

Ref. **2663**

🕒 3 weeks

Included in:

- ▶ Non-kinase enzyme profile
- ▶ Diversity profile
- ▶ Organ safety profile

Source  human recombinant

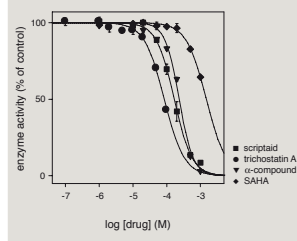
Substrate fluorogenic HDAC substrate class 2a (20 μ M)

Measured product fluoro-lysine

Detection method fluorimetry

Reference scriptaid (IC₅₀: 94 μ M)


Strahl, B.D. and Allis, C.D. (2000) *Nature*, **403**: 41-45.



sirtuin 1 (activator effect)

Ref. **2991**

🕒 3 weeks

Source  human recombinant (*E. coli*)

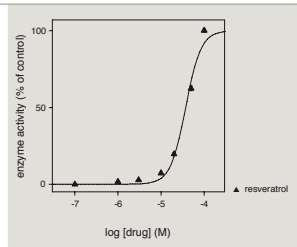
Substrate fluorogenic HDAC substrate (200 μ M)

Measured product fluoro-lysine

Detection method fluorimetry

Reference resveratrol (EC₅₀: 50 μ M)

Michan, S. and Sinclair, D. (2007) *Biochem. J.*, **404**: 1-13.




sirtuin 1 (inhibitor effect)

Ref. **2581**

🕒 3 weeks

Included in:

- ▶ Non-kinase enzyme profile
- ▶ Diversity profile
- ▶ Organ safety profile

Source  human recombinant (*E. coli*)

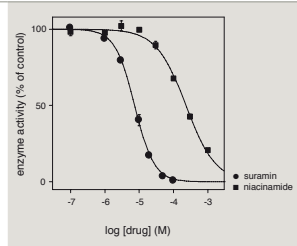
Substrate fluorogenic HDAC substrate (200 μ M)

Measured product fluoro-lysine

Detection method fluorimetry

Reference suramin (IC₅₀: 4.5 μ M)

Michan, S. and Sinclair, D. (2007) *Biochem. J.*, **404**: 1-13.




sirtuin 2

Ref. **2582**

🕒 3 weeks

Included in:

- ▶ Non-kinase enzyme profile
- ▶ Diversity profile
- ▶ Organ safety profile

Source  human recombinant (*E. coli*)

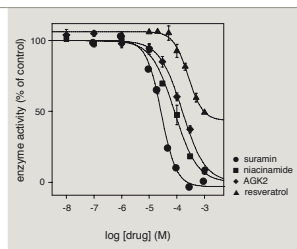
Substrate fluoro-lysine sirtuin 2 deacetylase substrate (150 μ M)

Measured product fluoro-lysine

Detection method fluorimetry

Reference suramin (IC₅₀: 26 μ M)


Michan, S. and Sinclair, D. (2007) *Biochem. J.*, **404**: 1-13.



sirtuin 3

Ref. **2583**

🕒 3 weeks

Source  human recombinant (*E. coli*)

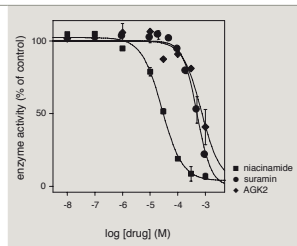
Substrate fluoro-lysine sirtuin 2 deacetylase substrate (20 μ M)

Measured product fluoro-lysine

Detection method fluorimetry

Reference niacinamide (IC₅₀: 31 μ M)

Michan, S. and Sinclair, D. (2007) *Biochem. J.*, **404**: 1-13.



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