

BACKGROUND

Histone acetylation/deacetylation alters chromosome structure, affects transcription factor access to DNA, and regulates gene expression.¹ Histone deacetylases (HDACs), as catalytic subunits of multiprotein complexes, deacetylate the ε-amino group of lysines located at the N-terminal tail of histones, resulting in the compaction of chromatin into a transcriptionally repressed state. In addition to the condensation of chromatin, HDACs deacetylate various proteins to regulate their function. Many of these proteins are transcription factors, such as p53, C/EBPβ, NF-κB and STATs. Therefore changes in the transcriptome upon HDAC inhibitor (HDACI) treatment can be due to a direct modulation of the "histone code" or the consequence of a rather indirect modulation of signaling pathways and transcription factor activities. HDACs have been shown to participate in a variety of cellular functions, including cell transformation, proliferation, senescence, differentiation, survival, and death.

Vertebrates express at least 18 distinct HDACs which have been grouped into four classes based on their similarity with yeast HDACs.² Class I HDACs (HDACs 1, 2, 3 and 8) are composed primarily of a catalytic domain. These HDACs are ubiquitously expressed, localized to the nucleus, and serve as transcriptional repressors. Class II HDACs (HDAC 4, 5, 6, 7, 9 and 10) are larger proteins with an extended N-terminus extension involved in protein-protein interactions. These HDACs are further sub-classified into Class IIa (HDACs 4, 5, 7, and 9) and IIb (HDACs 6 and 10). In contrast to Class I HDACs, Class II HDACs display stage and tissue-specific expression. These HDACs are able to shuttle in and out of the nucleus in response to certain cellular signals.

Phosphorylation of these HDACs at two N-terminal serine residues by the calcium-calmodulin-dependent kinase (CaMK) creates a docking site for 14-3-3 proteins, resulting in their export out of the nucleus. HDAC11 is the sole member of the Class III HDAC family. The fourth class of deacetylases, called sirtuins (SIRT1-7), has catalytic domains similar to the yeast NAD⁺-dependent deacetylase Sir2. While serving as HDACs in yeast, in mammalian cells SIRTs are involved in the deacetylation of proteins other than histones, and are therefore not considered to be "classical HDACs."

HDAC3 is located in both nuclear and cytoplasmic compartments as well as at the plasma membrane. It is required for cell growth and involved in the apoptotic process of almost all cell types via the regulation of pro-apoptotic genes. Moreover, HDAC3 has been suggested to have a role in the cytoplasm, notably in signal transduction since it is a substrate of the membrane associated tyrosine kinase Src. This

enzyme plays a critical role in development, inflammation and metabolism. It is present in specific complexes containing members of the nuclear receptor co-repressor family N-CoR/SMRT. HDAC3 is responsible for the deacetylation of lysine residues on the N-terminal part of the core histones that correlates with epigenetic repression. It can also target non-histone proteins. The activity of HDAC3 is regulated by the phosphorylation of the Ser424 residue of the protein and CK2 and PP4 are responsible for this regulation.³ The cleavage of the HDAC3 protein is another type of regulation affecting this enzyme.⁴

References:

1. de Ruijter AJ et al.: Biochem J. 370:737-49, 2003
2. Yang X and Seto E: Oncogene 26:5310-5318, 2007
3. Zhang, X. et al: Gene Dev. 19:827-39, 2005
4. Escaffit, F. et al: Mol. Cell. Biol. 27:554-67, 2006

TECHNICAL INFORMATION

Source:

HDAC3 Antibody is a mouse monoclonal antibody raised against purified recombinant human HDAC3 fragments expressed in E. coli.

Specificity and Sensitivity:

This antibody detects endogenous HDAC3 proteins without cross-reactivity with other family members.

Storage Buffer: PBS and 30% glycerol

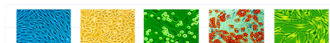
Storage:

Store at -20°C for at least one year. Store at 4°C for frequent use. Avoid repeated freeze-thaw cycles.

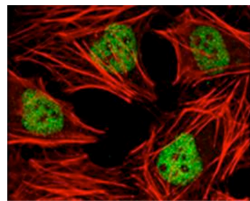
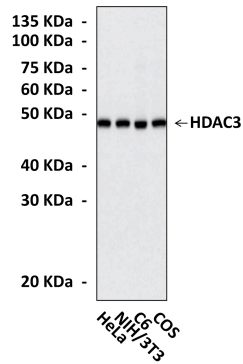
APPLICATIONS

Application:	*Dilution:
WB	1:1000
IP	1:50
IHC	1:200
ICC	1:200
FACS	n/d

**Optimal dilutions must be determined by end user.*



QUALITY CONTROL DATA



Top: Western Blot detection of HDAC3 proteins in various cell lysates using HDAC3 Antibody. **Bottom:** This antibody stains HeLa cells in confocal immunofluorescent analysis (HDAC3 antibody: Green; Actin filament: Red).

