

NSD1

CATALOG NO.: HMT-21-139

LOT NO.:

DESCRIPTION: Human recombinant NSD1 (residues 1538-2696 (end); Genbank Accession # NM_022455; MW = 130.9 kDa) expressed in Sf9 insect cells with an N-terminal His-tag. Catalyzes the transfer of methyl groups from S-adenosyl-L-methionine (SAM) to the ε-amino function of protein L-lysine residues, primarily producing the dimethyl form of lysine-36 of histone H3 (H3K36me2)^{1,2} but with activities also reported at H4K20^{3,4} and NF-κB p65 lysines 218 and 221⁵ (see also review⁶). While H3K36me2 is considered a gene-activating mark, NSD1 contains distinct domains that interact with liganded and unliganded nuclear receptors and can act as either a coactivator or corepressor⁷. NSD1 plays an essential role in early embryonic development³ and haploinsufficiency resulting from various NSD1 mutations can cause the developmental disorder Sotos syndrome^{8,9}. Chromosomal translocations resulting in the expression of a nucleoporin-98 (NUP98)-NSD1 fusion protein are implicated in the development of a subset of acute myeloid leukemias (AMLs)¹⁰ with a particularly poor prognosis¹¹, an oncogenic effect which requires NSD1's H3K36 methyltransferase activity and is associated with elevated expression of Hox-A genes¹². Chimeric NSD1 messages have also been detected in breast cancer cells¹³ and elevated NSD1 expression has been observed in metastatic melanoma cell lines¹⁴. A variety of results suggest a complex and context-dependent role for NSD1 in oncogenesis, including the elevated cancer risk in Sotos syndrome⁹, NSD1's tumor-suppressive effects in neuroblastoma⁴ and the fact that it is downregulated in primary prostate tumors (recurrent cancers), while upregulated in metastatic prostate tumors¹⁵.

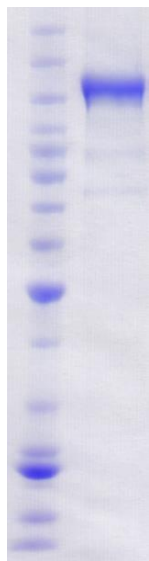
PURITY: >90% by SDS-PAGE

ASSAY CONDITIONS: RBC's NSD1 displays histone methyltransferase activity with HeLa oligo or mono/di-nucleosomes (0.05 mg/mL as [DNA]), 1 μM [³H]-SAM, 60 min. reactions, 30°C, as TCA-precipitated counts in a scintillation/filter plate assay (Multiscreen FB, Topcount). Reaction conditions are: 50 mM Tris-HCl, pH 8.5, 50 mM NaCl, 5 mM MgCl₂, 1 mM DTT, 1 mM PMSF, substrates at concentrations indicated above.

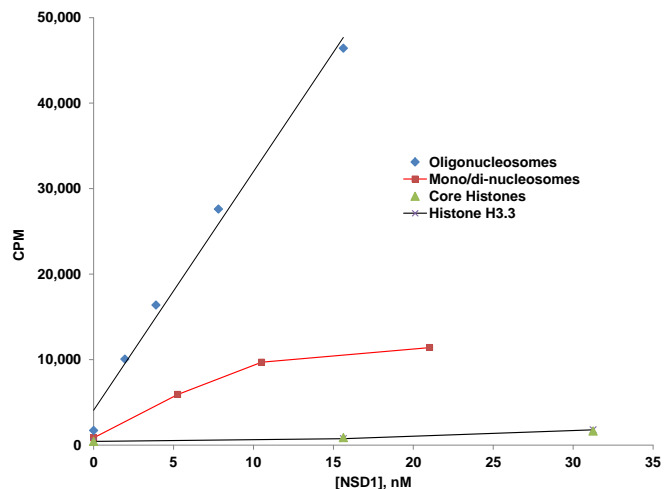
SUPPLIED AS: ___ μg/μl (total protein) in 50 mM Tris/HCl pH 7.5, 500 mM NaCl, 1 mM TCEP, 10% glycerol (v/v) as determined by OD₂₈₀

STORAGE: -70°C. Thaw quickly and store on ice before use. The remaining, unused, undiluted enzyme should be snap frozen, for example in a dry/ice ethanol bath or liquid nitrogen. Minimize freeze/thaws if possible, but very low volume aliquots (<5 μl) or storage of diluted enzyme is not recommended.

REFERENCES: 1) Y Li *et al. J. Biol. Chem.* 2009 **284** 34283; 2) Q. Qiao *et al. J. Biol. Chem.* 2011 **286** 8361; 3) G.V. Rayasam *et al. EMBO J.* 2003 **22** 3153; 4) M. Berdasco *et al. Proc. Natl. Acad. Sci USA* 2009 **106** 21830; 5) T. Lu *et al. Proc. Natl. Acad. Sci. USA* 2010 **107** 46; 6) M. Morishita & E. di Luccio *Biochim. Biophys. Acta* 2011 **412** 214; 7) N. Huang *et al. EMBO J.* 1998 **17** 3398; 8) N. Kurotaki *et al. Nat. Genet.* 2002 **30** 365; 9) G. Baujat & V. Cormier-Daire *Orphanet J. Rare Dis.* 2007 **2** 36; 10) R.J. Jaju *et al. Blood* 2001 **98** 1264; 11) I.H. Hollink *et al. Blood* 2011 **118** 3645; 12) G.G. Wang *et al. Nature Cell Biol.* 2007 **9** 804; 13) Q. Zhao *et al. Proc. Natl. Acad. Sci. USA* 2009 **106** 1886; 14) C.F. de Souza *et al. PLOS One* 2012 **7** e44800; 15) T. Bianco-Miotto *et al. Cancer Epidemiol. Biomarkers Prev.* 2010 **19** 2611



Coomassie blue stained SDS-PAGE (4-12% acrylamide) of 4 μg of purified NSD1. MW markers (left) are from top: 220, 160, 120, 100, 90, 80, 70, 60, 50, 40, 30, 25, 20, 15 and 10 kDa.



Methyltransferase Activity of NSD1. Assays were performed with a scintillation/filter plate assay. Incubations were 60 min., 30°C with HeLa mono/di-nucleosomes (RBC Cat. # HMT-35-123) or HeLa oligonucleosomes (RBC Cat. # HMT-35-130), both 0.05 mg/mL as [DNA], or chicken core histones (0.05 mg/mL) or histone H3.3 (1 μM; RBC Cat. # HMT-11-134) plus 1 μM [³H]-SAM.

This product is NOT intended for therapeutic or diagnostic use in animals or in humans.

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