

NSD2 (His)

(WHSC1, MMSET)

CATALOG NO.: HMT-21-138

LOT NO.:

DESCRIPTION: Human recombinant NSD2 (residues 2-1365 (end); Genbank Accession # NM_001042424; MW = 155.5 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, specifically lysine-36 of histone H3 (H3K36)¹ with, depending on substrate, activities also reported at H3K4², H4K20² and H4K44¹ (see also review³). NSD2's H4K20 methylation may be linked to double strand breaks and the DNA damage response⁴, whereas its principal regulatory functions appear to occur via methylation of H3K36^{5,6}, a mark associated with active transcription. NSD2 is overexpressed in multiple myelomas with the t(4;14) translocation⁷. NSD2 knockdown in such cells induces apoptosis⁵, while overexpression of catalytically active NSD2 promotes oncogenic transformation and tumor formation even in the absence of the translocation⁶. In addition to t(4;14)+ multiple myelomas, NSD2 expression is elevated in a variety of cancers (bladder^{8,9}, breast⁸, prostate⁸, kidney⁸, lung^{8,9}, pancreas⁸, colon⁹, stomach⁹, anal canal⁹, female genitals⁹, skin⁹, neuroblastoma¹⁰) and its carcinogenic effects may be mediated by interaction with β -catenin and effects on the WNT pathway⁸. Consequently, NSD2 is eliciting strong interest as a possible target for anti-cancer therapeutics^{3,8}.

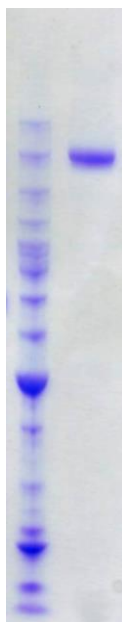
PURITY: >90% by SDS-PAGE

ASSAY CONDITIONS: RBC's NSD2 displays histone methyltransferase activity at concentrations of 15.6 nM-1 μ M, 60 min. reactions, 30°C, as TCA-precipitated counts in a scintillation/filter plate assay (Multiscreen FB, Topcount), with HeLa oligo or mono/di-nucleosomes (0.05 mg/mL as [DNA]). 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.

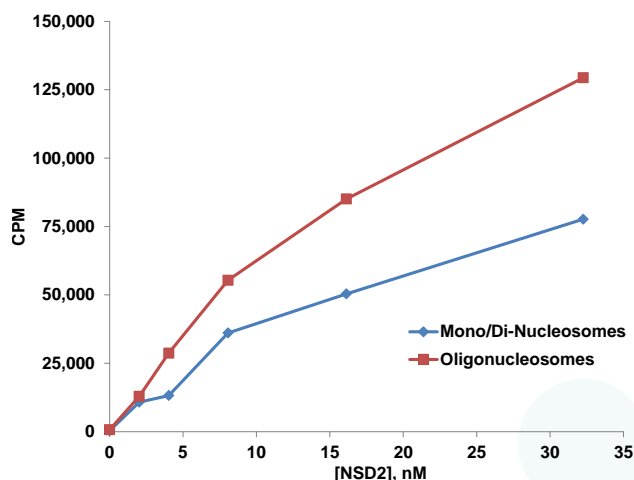
SUPPLIED AS: ___ μ M NSD2 (___ μ g/ μ l total protein) in 50 mM Tris/HCl pH 7.5, 500 mM NaCl, 1 mM TCEP, 10% glycerol (v/v) as determined by OD₂₈₀.

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 μ l) or storage of diluted enzyme is not recommended.

REFERENCES: 1) Y Li *et al. J. Biol. Chem.* 2009 **284** 34283; 2) J. Marango *et al. Blood* 2008 **111** 3145; 3) M. Morishita & E. di Luccio *Biochim. Biophys. Acta* 2011 **1816** 158; H. Pei *et al. Nature* 2011 **470** 124; 5) E. Martinez-Garcia *et al. Blood* 2011 **117** 211; 6) A.J. Kuo *et al. Mol. Cell* 2011 **44** 609; 7) J.J. Keats *et al. Blood* 2005 **105** 4060; 8) G. Toyokawa *et al. Neoplasia* 2011 **13** 887; 9) H.R. Hudlebusch *et al. Clin. Cancer Res.* 2011 **17** 2919; 10) H.R. Hudlebusch *et al. Cancer Res.* 2011 **71** 4226



Coomassie blue stained SDS-PAGE (4-12% acrylamide) of 2 μ g of purified NSD2 (His). MW markers at left, from top: 220, 160, 120, 100, 90, 80, 70, 60, 50, 40, 30, 25, 20, 15, & 10 kDa.



Methylation Activity of NSD2 with HeLa Mono/Di- and Oligonucleosomes. 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], and 1 μ M [³H]-SAM.

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

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