REACTION BIOLOGY

PRODUCT DATASHEET

NSD2 (WHSC1, MMSET)

CATALOG NO.: HMT-21-122 **LOT NO.:**

DESCRIPTION: Human recombinant NSD2 (residues 2-1365 (end); Genbank Accession # NM_001042424; MW = 152.5 kDa) expressed in *Sf9* insect cells with an N-terminal His-tag (removed during purification). 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 H3K4[2], H4K20[2] and H4K44[1] (see also review[3]). NSD2's H4K20 methylation may be linked to double strand breaks and the DNA damage response[4], 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) translocation[7]. NSD2 knockdown in such cells induces apoptosis[5], while overexpression of catalytically active NSD2 promotes oncogenic transformation and tumor formation even in the absence of the translocation[6]. In addition to t(4;14)+ multiple myelomas, NSD2 expression is elevated in a variety of cancers (bladder[8,9], breast[8], prostate[8], kidney[8], lung[8,9], pancreas[8], colon[9], stomach[9], anal canal[9], female genitals[9], skin[9], neuroblastoma[10]) and its carcinogenic effects may be mediated by interaction with ß-catenin and effects on the WNT pathway[8]. Consequently, NSD2 is eliciting strong interest as a possible target for anti-cancer therapeutics[3,8].

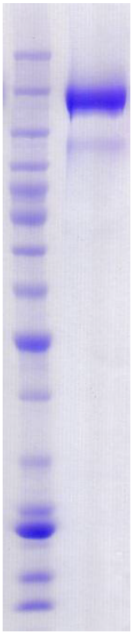
PURITY: >80% by SDS-PAGE

ASSAY CONDITIONS: RBC's NSD2 displays histone methyltransferase activity at concentrations of 15.6 nM-1 µM, 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 $MgCl_2$, 1 mM DTT, 1 mM PMSF, substrates at concentrations indicated above.

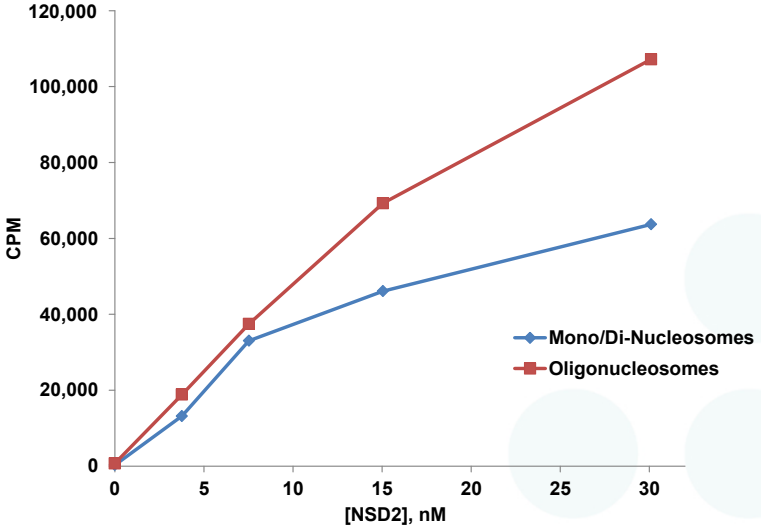
SUPPLIED AS: __ µM NSD2 (__ µg/µl total protein) in 50 mM Tris/HCl pH 7.5, 500 mM NaCl, 1 mM TCEP, 10% glycerol (v/v) as determined by OD_{280}.

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) 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 4 µg of RBC NSD2. MW markers (left) are, 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 µM [^{3}H]-SAM.

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