Recombinant Human Dkk-1 (Histidine-tagged)

Catalog Number: 1096-DK/CF

DESCRIPTION

Source	*Spodoptera frugiperda*, *Sf* 21 (baculovirus)-derived Thr32-His266 & Ser35-His266, both with a C-terminal 10-His tag Accession # O94907
N-terminal Sequence Analysis	Thr32 & Ser35
Predicted Molecular Mass	27 kDa

SPECIFICATIONS

SDS-PAGE	37 kDa, reducing conditions
Activity	Measured by its ability to interfere with the axis-inducing activity of Xwnt-8 mRNA in early *Xenopus* embryos. In a population of embryos, addition of 1 ng of rhDkk-1 per embryo resulted in 60-100% reduction in the number of secondary axes produced by 10-20 pg of Xwnt-8 mRNA. Measured by its ability to inhibit Wnt-3a-induced alkaline phosphatase production by MC3T3−E1 mouse preosteoblast cells. The ED_{50} for this effect is typically 0.3-1.2 µg/mL in the presence of 10 ng/mL of Wnt-3a. **Optimal concentrations should be determined by each laboratory for each application.**
Endotoxin Level	<1.0 EU per 1 µg of the protein by the LAL method.
Purity	>90%, by SDS-PAGE under reducing conditions and visualized by silver stain.
Formulation	Lyophilized from a 0.2 µm filtered solution in Tris-Citrate and NaCl. See Certificate of Analysis for details.

PREPARATION AND STORAGE

Reconstitution	Reconstitute at 100 µg/mL in sterile PBS.
Shipping	The product is shipped at ambient temperature. Upon receipt, store it immediately at the temperature recommended below.
Stability & Storage	**Use a manual defrost freezer and avoid repeated freeze-thaw cycles.** ● 12 months from date of receipt, -20 to -70 °C as supplied. ● 1 month, 2 to 8 °C under sterile conditions after reconstitution. ● 3 months, -20 to -70 °C under sterile conditions after reconstitution.

BACKGROUND

Dickkopf related protein 1 (Dkk-1) is a member of the Dkk protein family that includes Dkk-1, -2, -3, and -4 (1). All four members are secreted proteins that are synthesized as precursor proteins with an N-terminal signal peptide and 2 conserved cysteine-rich domains, which are separated by a linker region. Dkk proteins have potential furin type proteolytic cleavage sites, and short forms of Dkk-2 and Dkk-4 containing only the second cysteine-rich domain can be generated by proteolytic processing (1). Dkk proteins have distinct patterns of expression in adult and embryonic tissues, suggesting that they may play diverse roles in these tissues.

The Dkk proteins have distinct effects on Wnt signaling. Dkk-1 and Dkk-4 are Wnt antagonists. Dkk-3 has not been demonstrated to affect Wnt signaling, and Dkk-2 acts as an agonist or antagonist, depending on the cellular context. Wnt signaling regulates many important developmental processes including neural crest differentiation, brain development, kidney morphogenesis, and sex determination. In addition, Wnt signaling has also been implicated in tumor formation. Canonical Wnt signaling via the beta-catenin pathway is transduced by a receptor complex composed of the Frizzled proteins (Fz) and low-density lipoprotein (LDL) receptor-related proteins (LRP5/6) (2, 3). Unlike many soluble Wnt antagonists that function by binding extracellular Wnt ligands to prevent interaction of Wnt with the Fz-LRP5/6 receptor complex, Dkk-1 and Dkk-4 antagonize Wnt/beta-catenin signaling by direct high-affinity binding to the Wnt coreceptor LRP5/6 and inhibiting interaction of LRP5/6 with the Wnt-Frizzled complex (4). Dkk-1 and Dkk-4 also bind the transmembrane proteins Kremen1 (Krm1) and Krm2 with high-affinity (5). Krm2 has been shown to form a ternary complex with Dkk-1 or -4 and LRP5/6 to trigger internalization of the complex and removal LRP6 from the cell surface. Thus, Dkk-1/4 and Kremens function synergistically to antagonize LRP5/6-mediated Wnt activity. Dkk-2 also binds to LRP5/6 and the Kremens, but Dkk-2 acts as antagonist of the Wnt signaling pathway only in the presence of Krm2 (5, 6). Dkk-2 binding to LRP5/6 in the absence of Krm2 activates rather than inhibits Wnt signalling (6).

References:

1. Krupnik, V.E. *et al.* (1999) Gene **238**:301.
2. Zorn, A.M (2001) Current Biology R592.
3. Mao, J. *et al.* (2001) Mol. Cell **7**:801.
4. Nusse, R. *et al.* (2001) Nature **411**:255.
5. Mao, J. *et al.* (2002) Nature **417**:664.
6. Mao, B. and C. Niehrs (2003) Gene **302**:179.