

DESCRIPTION

Source Mouse myeloma cell line, NS0-derived mouse DLL4 protein
Ser28-Pro525, with a C-terminal 10-His tag
Accession # BAB18580

N-terminal Sequence Analysis Ser28

Predicted Molecular Mass 55.6 kDa

SPECIFICATIONS

SDS-PAGE 75-80 kDa, reducing conditions

Activity Measured by the ability of the immobilized protein to enhance BMP-2 induced alkaline phosphatase activity in C3H10T1/2 mouse embryonic fibroblast cells. Nobta, M. *et al.* (2005) *J. Biol. Chem.* **280**:15842.
The ED₅₀ for this effect is 150-600 ng/mL.

Endotoxin Level <0.10 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-HCl, NaCl and PEG3350. See Certificate of Analysis for details.

PREPARATION AND STORAGE

Reconstitution Reconstitute at 200 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

Delta-like protein 4 (DLL4) is a type I membrane protein belonging to the Delta/Serrate/Lag2 (DSL) family of Notch ligands (1). Notch signaling is an evolutionarily conserved pathway that controls cell fate and is required in multiple developmental processes including vascular development, hematopoiesis, somatogenesis, myogenesis, and neurogenesis (2 - 4). Dysregulation in the Notch pathway is associated with various human diseases. In mammals, four Notch homologs (Notch 1 to 4) and five ligands (DLL 1, 3 and 4, Jagged 1 and 2) have been identified. Notch ligands are transmembrane proteins with a DSL motif necessary for Notch binding, tandem EGF repeats, a transmembrane region and a short intracellular domain (ICD). Notch ligands are categorized into two subfamilies based on the presence of an extracellular cysteine-rich domain and insertions that interrupt some EGF repeats in the Jagged but not the Delta ligand family. Interactions of Notch receptors with their ligands results in reciprocal regulated intramembrane proteolysis (RIP) (4). RIP is a mechanism for transmembrane signal transduction that involves the sequential processing by a disintegrin metalloprotease (ADAM) and then by presenilin/γ secretase, resulting in shedding of the extracellular domains and the generation of the soluble ICD signaling fragments, respectively. The Notch ICD translocates to the nucleus and interacts with transcriptional coactivators, resulting in the transcription of target genes. The ICDs of the Notch ligands have also been shown to translocate to the nucleus where they may have a signaling function (5, 6). DLL4 is expressed highly and selectively within the arterial endothelium and has been shown to function as a ligand for Notch 1 and Notch 4. Human and mouse DLL4 share 86% amino acid sequence identity (1).

References:

1. Shutter, J.R. *et al.* (2000) *Genes Dev.* **14**:1313.
2. Iso, Tatsuya *et al.* (2002) *Arterioscler. Thromb. Vasc. Biol.* **23**:543.
3. Walker, L. *et al.* (2001) *Stem Cells* **19**:543.
4. Baron, M. (2002) *Semin. Cell Dev. Biol.* **14**:113.
5. Ikeuchi, T. and S.S. Sisodia (2003) *J. Biol. Chem.* **278**:7751.
6. Bland, C.E. *et al.* (2003) *J. Biol. Chem.* **278**:13607.