

DLL4 Protein, Human, Recombinant (His & Avi), Biotinylated

General Information

Synonyms:	hδ2;δ-like 4;Delta-like 4;δ-like 4 (Drosophila);delta-like 4 (Drosophila);hdelta2
Protein Construction:	A DNA sequence encoding the human DLL4 (NP_061947.1) (Met1-Pro524) was expressed with a C-terminal polyhistidine tag followed by an AVI tag. The expressed protein was biotinylated in vivo by the Biotin-Protein ligase (BirA enzyme) which is co-expressed. Predicted N terminal: Ser 27
Species:	Human
Expression Host:	HEK293 Cells
Accession:	NP_061947.1
Molecular Weight:	57.55 kDa (predicted); 66.88 kDa (reducing conditions)

QC Testing

Biological Activity:	Immobilized Recombinant Human NOTCH1 Protein (Fc Tag) at 2 µg/mL (100 µL/well) can bind Recombinant Human DLL4 Protein (His & AVI Tag), Biotinylated with a linear range of 0.25-2.2 µg/mL.
Purity:	≥ 95 % as determined by SDS-PAGE. ≥ 95 % as determined by SEC-HPLC.
Endotoxin:	< 1.0 EU/µg of the protein as determined by the LAL method.
Formulation:	Lyophilized from a solution filtered through a 0.22 µm filter, containing PBS, pH 7.4. Typically, a mixture containing 5% to 8% trehalose, mannitol, and 0.01% Tween 80 is incorporated as a protective agent before lyophilization.

Preparation and Storage

Reconstitution:
A Certificate of Analysis (CoA) containing reconstitution instructions is included with the products. Please refer to the CoA for detailed information.

Stability & Storage:

It is recommended to store recombinant proteins at -20°C to -80°C for future use. Lyophilized powders can be stably stored for over 12 months, while liquid products can be stored for 6-12 months at -80°C. For reconstituted protein solutions, the solution can be stored at -20°C to -80°C for at least 3 months. Please avoid multiple freeze-thaw cycles and store products in aliquots.

Actual storage temperature shall be subject to the COA.

Shipping:

In general, lyophilized powders are shipped with blue ice, while solutions are shipped with dry ice.

Protein Background

Delta-like protein 4 (DLL4, Delta4), a type I membrane-bound Notch ligand, is one of five known Notch ligands in mammals and interacts predominantly with Notch 1, which has a key role in vascular development. Recent studies

yield substantial insights into the role of DLL4 in angiogenesis. DLL4 is induced by vascular endothelial growth factor (VEGF) and acts downstream of VEGF as a 'brake' on VEGF-induced vessel growth, forming an autoregulatory negative feedback loop inactivating VEGF. DLL4 is downstream of VEGF signaling and its activation triggers a negative feedback that restrains the effects of VEGF. Attenuation of DLL4/Notch signaling results in chaotic vascular network with excessive branching and sprouting. DLL4 is widely distributed in tissues other than vessels including many malignancies. Furthermore, the molecule is internalized on binding its receptor and often transported to the nucleus. In pathological conditions, such as cancer, DLL4 is up-regulated strongly in the tumour vasculature. Blockade of DLL4-mediated Notch signaling strikingly increases nonproductive angiogenesis, but significantly inhibits tumor growth in preclinical mouse models. In preclinical studies, blocking of DLL4/Notch signaling is associated with a paradoxical increase in tumor vessel density, yet causes marked growth inhibition due to functionally defective vasculature. Thus, DLL4 blockade holds promise as an additional strategy for angiogenesis-based cancer therapy.

Reference

- Yan M, et al. (2007) Delta-like 4/Notch signaling and its therapeutic implications. *Clin Cancer Res.* 13(24): 7243-6.
- Sainson RC, et al. (2007) Anti-Dll4 therapy: can we block tumour growth by increasing angiogenesis? *Trends Mol Med.* 13(9): 389-95.
- Martinez JC, et al. (2009) Nuclear and membrane expression of the angiogenesis regulator delta-like ligand 4 (DLL4) in normal and malignant human tissues. *Histopathology.* 54(5): 598-606.
- Li J, et al. (2010) Targeting DLL4 in tumors shows preclinical activity but potentially significant toxicity. *Future Oncol.* 6(7): 1099-103.

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