

DESCRIPTION

Source	Chinese Hamster Ovary cell line, CHO-derived human DLL4 protein		
	Human DLL4 (Ser27-Pro524) Accession # Q9NR61.1	IEGRMD	Human IgG ₁ (Pro100-Lys330)
	N-terminus		C-terminus
N-terminal Sequence Analysis	Ser 27		
Structure / Form	Disulfide-linked homodimer		
Predicted Molecular Mass	81 kDa		

SPECIFICATIONS

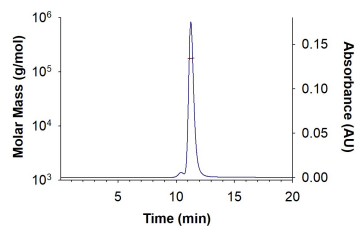
SDS-PAGE	89-98 kDa, under reducing conditions.
Activity	Measured by its binding ability in a functional ELISA. Recombinant Human DLL4 Fc Chimera (Catalog # BT-DLL4) binds to Recombinant Human Notch-1 Fc Chimera (Catalog # 3647-TK) with an ED ₅₀ of 2.00-20.0 ng/mL.
Endotoxin Level	<0.10 EU per 1 µg of the protein by the LAL method.
Purity	>95%, by SDS-PAGE with quantitative densitometry by Coomassie® Blue Staining.
Formulation	Lyophilized from a 0.2 µm filtered solution in HBS and Tween®-80 with Trehalose. See Certificate of Analysis for details.

PREPARATION AND STORAGE

Reconstitution	Reconstitute the 20 µg size at 100 µg/mL in water. Reconstitute all other sizes at 500 µg/mL in water.
Shipping	The product is shipped at ambient temperature. Upon receipt, store it immediately at the temperature recommended below.
Stability & Storage	<p>Use a manual defrost freezer and avoid repeated freeze-thaw cycles.</p> <ul style="list-style-type: none"> • 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.

DATA

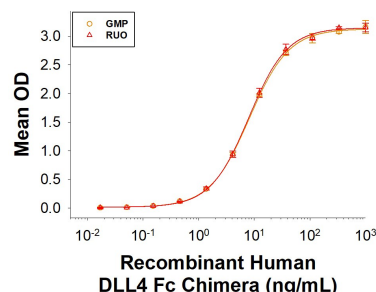
SEC-MALS



Recombinant Human DLL4 Fc Chimera Protein SEC-MALS. Recombinant Human DLL4 Fc Chimera Protein (Catalog # BT-DLL4) has a molecular weight (MW) of 168-185 kDa as analyzed by SEC-MALS, suggesting that this protein is a homodimer. MW may differ from predicted MW due to post-translational modifications (PTMs) present (i.e. Glycosylation).

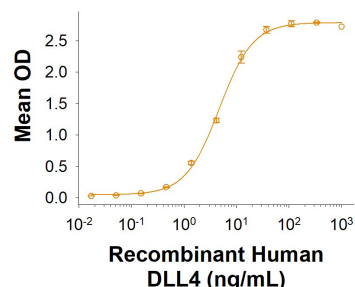
SEC-MALS Data	Result
Retention Time	10.7 - 12.7 min
MW - Predicted (Monomer)	80.9 kDa
MW - MALS	176.4 kDa
Polydispersity	1.007
System Suitability	Pass
IMA Monomer 66.4 ± 3.32 kDa	

Binding Activity



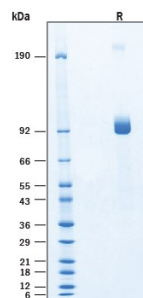
Equivalent Binding Activity of GMP and RUO grades of Recombinant Human DLL4. Equivalent binding activity of GMP (Catalog # BT-DLL4-GMP) and RUO (Catalog # BT-DLL4) grades of Recombinant Human DLL4 as measured in a functional ELISA with Recombinant Human Notch-1 Protein (orange and red, respectively).

Binding Activity



Recombinant Human DLL4 Fc Chimera Protein Binding Activity. In a functional ELISA, Recombinant Human DLL4 Fc Chimera Protein (Catalog # BT-DLL4) binds to Recombinant Human Notch-1 Fc Chimera (Catalog # 3647-TK) with an ED₅₀ of 2.00-20.0 ng/mL.

SDS-PAGE



Recombinant Human DLL4 Fc Chimera Protein SDS-PAGE. 2 µg/lane of Recombinant Human DLL4 Fc Chimera Protein (Catalog # BT-DLL4) was resolved with SDS-PAGE under reducing (R) condition and visualized by Coomassie® Blue staining, showing bands at 89-98 kDa.

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/ gamma 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). The use of DLL4, in conjunction with VCAM1, has been shown as an effective method for generating hematopoietic progenitors and T cells from hPSCs in a serum- and feeder-free environment.

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.