PRODUCT INFORMATION

4-1BB Ligand Extracellular Domain (human, recombinant)

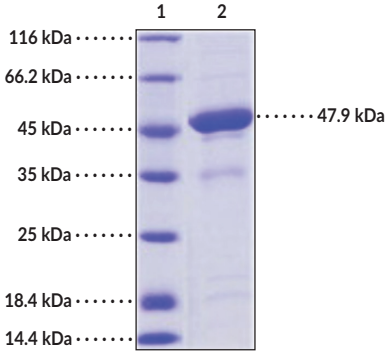
Item No. 32067

Overview and Properties

Synonyms:	4-1BBL, CD137L, CD137 Ligand, TNFSF9
Source:	Active recombinant N-terminal human IgG1 Fc-tagged 4-1BB ligand expressed in HEK293 cells
Amino Acids:	71-254
Uniprot No.:	P41273
Molecular Weight:	47.9 kDa
Storage:	-80°C (as supplied)
Stability:	≥1 year
Purity:	≥85% estimated by SDS-PAGE
Supplied in:	Lyophilized from sterile PBS, pH 7.4
Endotoxin Testing:	<1.0 EU/µg, determined by the LAL endotoxin assay
Bioactivity:	See figures for details

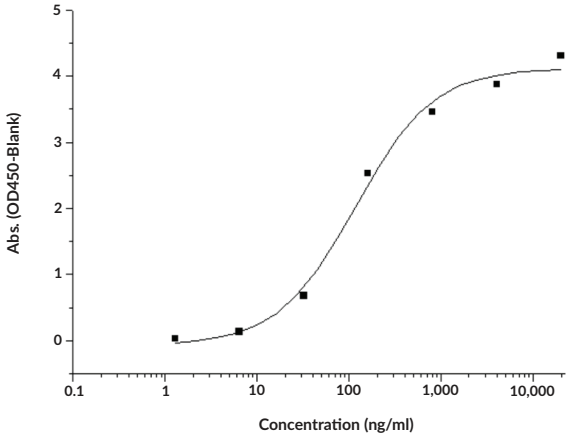
Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Images



Lane 1: MW Markers
Lane 2: 4-1BB Ligand Extracellular Domain

SDS-PAGE Analysis of 4-1BB Ligand Extracellular Domain.



4-1BB Ligand Extracellular Domain Binding in a Functional ELISA. Immobilized 4-1BB at 10 µg/ml can bind 4-1BB Ligand Extracellular Domain, the EC_{50} value for this effect is 7-40 ng/ml.

CAYMAN CHEMICAL
1180 EAST ELLSWORTH RD
ANN ARBOR, MI 48108 · USA
PHONE: [800] 364-9897
[734] 971-3335
FAX: [734] 971-3640
CUSTSERV@CAYMANCHEM.COM
WWW.CAYMANCHEM.COM

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Description

TNF ligand superfamily member 9 (4-1BB ligand) is a type II transmembrane glycoprotein and a member of the TNF superfamily.[1,2] It is composed of an N-terminal cytoplasmic region, a transmembrane domain, and a C-terminal extracellular tail region that contains a TNF homology domain.[2,3] 4-1BB ligand production is induced in antigen-presenting cells (APCs), such as dendritic cells, B cells, and macrophages, by CD40 and toll-like receptor (TLR) activation.[2] It forms homotrimers and binds to its receptor, 4-1BB, on antigen-primed T cells, which induces NF-κB and MAPK signaling through TNF receptor-associated factors (TRAFs) and, when the T cell is co-stimulated by other factors, induces PI3K-Akt signaling.[1,2] This action promotes the proliferation of T cells, production of cytokines, and cell survival.[2] Soluble forms of 4-1BB ligand, consisting of only the extracellular domain, also form trimers that bind to its receptor but do not induce signaling.[4] Mice deficient for 4-1BB ligand, *Tnfsf9*, have impairments in the formation of $CD8^+$ T cell memory cells and in clearing pathogens.[2,5] *Tnfsf9* knockout mice also develop B cell lymphomas before 12 months of age.[6] 4-1BB ligand antibodies induce T regulatory cell expansion and prevent allogeneic graft rejection of pancreatic islets in mice.[7] Intratumoral adenovirus-mediated gene transfer of *Tnfsf9* induces tumor regression in a mouse syngeneic model of breast cancer.[6] The protein levels of 4-1BB ligand are elevated in more than 40% of patients with acute myeloid leukemia (AML) or non-Hodgkin's lymphoma but the expression of *TNFSF9* is either elevated or reduced in cancer patients depending on the type of cancer. Cayman's 4-1BB Ligand Extracellular Domain (human, recombinant) protein can be used for ELISA and binding assay applications. This protein is a disulfide-linked homodimer. The reduced monomer, comprised of 4-1BB ligand (amino acids 71-254) fused to human IgG1 Fc at the N-terminus, consists of 444 amino acids and has a calculated molecular weight of 47.9 kDa.

References

1. Barsoumian, H.B., Batra, L., Shrestha, P., *et al.* A novel form of 4-1BBL prevents cancer development via nonspecific activation of $CD4^+$ T and natural killer cells. *Cancer Res.* **79(4)**, 783-794 (2019).
2. So, T. and Ishii, N. The TNF–TNFR family of co-signal molecules. *Co-signal molecules in T cell activation.* Azuma, M. and Yagita, H., editors, 1st edition, *Springer Singapore* (2019).
3. Bitra, A., Doukov, T., Croft, M., *et al.* Crystal structures of the human 4-1BB receptor bound to its ligand 4-1BBL reveal covalent receptor dimerization as a potential signaling amplifier. *J. Biol. Chem.* **293(26)**, 9958-9969 (2018).
4. Wyzgol, A., Müller, N., Fick, A., *et al.* Trimer stabilization, oligomerization, and antibody-mediated cell surface immobilization improve the activity of soluble trimers of CD27L, CD40L, 41BBL, and glucocorticoid-induced TNF receptor ligand. *J. Immunol.* **183(3)**, 1851-1861 (2009).
5. Wang, C., Lin, G.H.Y., McPherson, A.J., *et al.* Immune regulation by 4-1BB and 4-1BBL: Complexities and challenges. *Immunol. Rev.* **229(1)**, 192-215 (2009).
6. Vinay, D.S. and Kwon, B.S. Immunotherapy of cancer with 4-1BB. *Mol. Cancer Ther.* **11(5)**, 1062-1070 (2012).
7. Elpek, K.G., Yolcu, E.S., Franke, D.D.H., *et al.* Ex vivo expansion of $CD4^+CD25^+FoxP3^+$ T regulatory cells based on synergy between IL-2 and 4-1BB signaling. *J. Immunol.* **179(11)**, 7295-7304 (2007).

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