

Background Information

4-1BB ligand (4-1BBL; also CD137L) is a 32 kDa type II transmembrane protein that belongs to TNF superfamily (TNFSF) of molecules.¹⁻⁴ The human 4-1BBL cDNA encodes a 254 amino acid (aa) protein that contains a 25 aa N-terminal cytoplasmic domain, a 23 aa transmembrane segment, and a 206 aa C-terminal extracellular region.⁵ The extracellular domain (ECD) of 4-1BBL has a jelly-roll, β -sandwich tertiary structure that is similar to other TNFSF members. There is only one cysteine in the human ECD, and no potential N-linked glycosylation sites. The potential exists, however, for O-linked glycosylation. The human 4-1BBL ECD shares 32% and 35% aa identity with mouse and rat ECD, respectively. In the cytoplasmic domain, human 4-1BBL is 55 aa shorter than the equivalent region in rodents. 4-1BBL is expressed by activated B cells, macrophages, dendritic cells, activated T cells, neurons, and astrocytes.^{2,3,6} A 26 kDa soluble form of 4-1BBL is known to occur in human. Although it is presumably generated by MMP activity, its amino acid size is currently unreported.⁴ The soluble form is bioactive. Human 4-1BBL signals through both CD137/4-1BB and itself. Its cytoplasmic tail participates in reverse signaling that induces apoptosis in T cells and cytokine secretion (IL-6; TNF- α) by monocytes.^{7,8} 4-1BBL binding to CD137/4-1BB produces a number of effects. It seems to play a key role in the T cell recall response. It maintains T cell numbers at the end of a primary response, and induces CD4⁺ and CD8⁺ T cells to proliferate and secrete cytokines such as IL-2 and IFN- γ in CD4⁺ cells, and IFN- γ in CD8⁺ cells.^{9,10}

References

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Warning: Contains sodium azide as a preservative - sodium azide may react with lead and copper plumbing to form explosive metal azides. Flush with large volumes of water during disposal.