

The B7-CD28 Superfamily

The B7 family of ligands and the CD28 family of receptors belong to the Immunoglobulin SuperFamily (IgSF). Interactions between B7 ligands and CD28 receptors play an essential role in regulating T-cell response by eliciting both positive co-stimulatory and negative inhibitory signals. There are currently seven known members of the B7 family: B7-1 (CD80), B7-2 (CD86), Inducible T cells Co-Stimulator Ligand (ICOSL), Programmed cell Death protein Ligand 1 (PD-L1), PD-L2, B7-H3, and B7-H4 and five known members of the CD28 family: CD28, CTLA4, ICOS, PD1 and B- and T-Lymphocyte Attenuator (BTLA).

Human ICOS

Inducible T-cell costimulator (ICOS) is a T-cell-specific, surface receptor of the immunoglobulin superfamily that binds inducible costimulatory ligand (ICOSL), alternatively referred to as B7-H2, to play a critical role in the development and function of regulatory T-cells (Tregs). ICOS joins CD28, CTLA-4 and PD-1 as a member of the growing CD28/CTLA-4 family of costimulatory immunoreceptors that function synergistically with members of the B7 family of transmembrane ligands, including B7-1, B7-2, B7-H1 (PD-L1), B7-H2 and PD-L2, to constitute crucial costimulatory pathways for T-cell and B-cell regulatory responses. As the main receptor of B7-H2, ICOS can have both negative and positive influence over immune response, including the direct downregulation of B7-H2, and is critically involved in the immunosuppression of tumor-associated memory CD4+ T-cells. Interaction between ICOS and B7-H2 on the surface of antigen presenting cells potentiates costimulatory signals responsible for enhancing basic T-cell response to foreign antigens, namely the augmentation of T-cell proliferation, the upregulation of molecules responsible for mediating intercellular interaction, and the secretion of cytokines such as IL-4, IL-10 and IL-21. The significant involvement of ICOS and B7-H2 interaction within an array of immunological responses, such as those of Th1, Th2 and Th17 cells, means that the blockade of this interaction has been linked to a number of autoimmune diseases, including rheumatoid arthritis (RA), inflammatory bowel disease (IBD), type 1 diabetes, and graft versus host disease (GVHD). Unlike CD28, which is constitutively expressed on the surface of T-cells where it has restricted interaction with B7-H2, ICOS is expressed at low levels on naive T-cells and is upregulated on activated T-cells and regulatory T-cells (Tregs) after TCR ligation and CD28 stimulation. PeproTech's CHO cell-derived Recombinant Human ICOS Fc is a glycosylated, homodimer 79.4 kDa of 706 amino acid residues whose monomer consists of the 120-amino-acid-length extracellular portion of ICOS fused to the 231-amino-acid-length Fc portion of human IgG1 by two glycines. The calculated molecular weight of Recombinant Human ICOS Fc dimer is 79.4 kDa; however, due to glycosylation, it migrates at an apparent molecular weight of approximately 40-45 kDa by SDS-PAGE analysis under reducing conditions.

Human PD-1

Programmed cell death protein 1 (PD-1), or CD279, is a type I inhibitory transmembrane receptor of the CD28 receptor family that, along with its B7 family ligands, programmed death ligand 1 (PD-L1) and programmed death ligand 2 (PD-L2), belongs to the immunoglobulin superfamily. While other CD28 family members are expressed predominantly in T cells, PD-1 is widely expressed and found in multiple lymphocytes including T cells, B cells, myeloid, and NKT cells upon activation. PD-1 is a negative regulator of immune response, and is referred to as an inhibitory immune checkpoint molecule. Ligation with PD-L1 or PD-L2 results in inhibited activation, proliferation, and cytokine secretion (e.g. IFN-gamma, IL-10) in T cells, ultimately dampening immune response. Despite the strong homology between PD-L1 and PD-L2, each ligand appears to display distinct lymphokine expression patterns and potency. Blockage of PD-1 ligation by monoclonal antibodies has been proven to be an effective anti-tumor treatment by allowing the immune response to remain active and attack the tumorigenic cells that otherwise would have escaped detection. PD-1 and its ligands have been implicated in numerous autoimmune diseases, inflammatory liver disease and cancers. The naturally occurring human PD-1 monomer consists of a 150 amino acid extracellular domain, a 21 amino acid transmembrane domain, and a 97 amino acid cytoplasmic domain. PeproTech's CHO cell-derived Recombinant Human PD-1 Fc is a glycosylated, disulfide-linked homodimer of 501 amino acid residues whose monomer consists of the 268-amino-acid length mature PD-1 sequence fused to the 231-amino-acid length Fc portion of human IgG1 by two glycines. The calculated molecular weight of monomeric CHO cell-derived Recombinant Human PD-1 Fc is 55.3 kDa, however, due to glycosylation, it migrates at an apparent molecular weight of approximately 180-200 kDa by SDS-PAGE analysis under non-reducing conditions.

Recombinant Human PD-1 Fc

Catalog Number: 310-40

Human PD-L2

Programmed death-ligand 2 (PD-L2), or B7-DC, is a member of the B7 ligand family within the immunoglobulin superfamily that, along with programmed death-ligand 1 (PD-L1), acts as a ligand for programmed cell death protein 1 (PD-1). Though expressed primarily in dendritic cells, PD-L2 expression can be induced on a wide variety of immune and non-immune cells depending on the microenvironment. PD-L2 expression is particularly upregulated in the presence of Th2 cytokine, IL-4, as well as Th1 cytokines, TNF- α and IFN- γ to a lesser degree. While generally expressed at lower levels compared to PD-L1, PD-L2 demonstrates a 2 to 6 times higher relative affinity to PD-1 than PD-L1. PD-1 and its ligands are referred to as inhibitory immune checkpoint molecules in that they provide useful negative feedback during physiological homeostasis.

The B7-CD28 Superfamily (cont'd)

Ligation of PD-L2 or PD-L1 inhibits activation, proliferation, and cytokine secretion (e.g. IFN-gamma, IL-10) in T cells, ultimately dampening immune response. Conversely, studies have shown that PD-L2 can also stimulate T-cell proliferation and cytokine production, even in PD-1-deficient T cells, suggesting additional receptors. Recent studies have concluded that PD-L2 also binds to a second receptor, repulsive guidance molecule b (RGMb), which was originally identified as a receptor for bone morphogenetic proteins (BMPs). RGMb is expressed in the central nervous system, as well as in macrophages, however, its role in immunity is only beginning to emerge. Interaction between PD-L2 and RGMb regulates the development of respiratory tolerance in the lung through BMP and/or neogenin signaling pathways. The naturally occurring human PD-L2 monomer consists of a 201-amino-acid extracellular domain, a 21-amino-acid transmembrane domain, and a 32-amino-acid cytoplasmic domain. PeproTech's CHO cell-derived Recombinant Human PD-L2 Fc is a glycosylated, disulfide-linked homodimer of 433-amino-acid residues whose monomer consists of a 200-amino-acid portion of mature PD-L2, including Leu20 through Pro219, fused to the 231-amino-acid length Fc portion of human IgG1 by two glycines. The calculated molecular weight of monomeric CHO cell-derived Recombinant Human PD-L2 Fc is 48.6 kDa; however, due to glycosylation, it migrates at an apparent molecular weight of approximately 65-75 kDa by SDS-PAGE analysis under reducing conditions.

Recombinant Human PD-L2 Fc

Catalog Number: 310-38

Additional B7-CD28 Superfamily Products Offered by PeproTech

Product	Catalog Number
Recombinant Human B7-1 Fc (CD80)	310-32
Recombinant Human B7-2 Fc (CD86)	310-33
Recombinant Human B7-H2 Fc (ICOSL)	310-37
Recombinant Human sCD28 Fc	310-34
Recombinant Human TMIGD2/CD28H Fc	310-42
Recombinant Human CTLA-4 Fc	310-05
Recombinant Human PD-L1 Fc	310-35

