

Product Information

BONE MORPHOGENETIC PROTEIN RECEPTOR IB (BMPR-IB)/Fc Chimera

Human, Recombinant
Expressed in mouse NSO cells

Product Number **B 3305**

Product Description

Bone Morphogenetic Protein Receptor IB (BMPR-IB)/Fc Chimera is produced from the DNA sequence encoding the signal peptide from human CD33 (Met 1 - Met 17) joined with Lys 14 - Arg 126 from the extracellular domain of human BMPR-IB.¹ The protein is fused to the carboxy-terminal 6X histidine-tagged Fc region of human IgG1 by a polypeptide linker. Recombinant human BMPR-IB, generated after the removal of amino acid residues 1 -17 from the CD33 signal peptide, is a disulfide-linked homodimeric protein comprised of two 357 amino acid residues. The calculated molecular mass of is approximately 40 kDa. Due to glycosylation, the recombinant protein migrates as a 50 to 55 kDa protein in SDS-PAGE. Human and mouse BMPR-IB are highly conserved and share 98 % amino acid sequence identity.

Bone Morphogenetic Proteins (BMP) are members of the TGF- β superfamily of cytokines that affect bone and cartilage formation.^{2, 3, 4} Similar to other TGF- β family proteins, BMPs are highly conserved across animal species. Mature BMPs are 30-38 kDa proteins that assume a TGF- β -like cysteine knot configuration. Unlike TGF- β , BMPs do not form latent complexes with their propeptide counterparts. Most BMPs are homodimers, but bioactive natural heterodimers have been reported. Recently it was found that lovostatin (Mevinolin, Sigma Product M 2147), widely used for lowering cholesterol, also increases bone formation by turning on a gene (*bmp-2*) that promotes local bone formation.⁵ BMPs are involved in embryogenesis and morphogenesis of various tissues and organs. They create an environment conducive for bone marrow development by stimulating the production of specific bone matrix proteins and altering stromal cell and osteoclast proliferation.^{6, 7} In addition to stimulating ectopic bone and cartilage development, BMPs may be an important factor in the development of the viscera. BMPs regulate the growth, differentiation, chemotaxis, proliferation, and apoptosis of various cell types, including mesenchymal cells, epithelial cells, hemato-

poietic cells, and neuronal cells.^{2, 8} BMPs also appear to be responsible for normal dorsal/ventral patterning and can found in tissues that induce bone or cartilage growth such as demineralized bone and urinary epithelium.

Cellular responses to BMPs are mediated by the formation of hetero-oligomeric complexes of the type I and type II serine/threonine kinase receptors⁹ which play significant roles in BMP binding and signaling. Bone Morphogenetic Protein Receptor IB (BMPR-IB), also known as activin receptor-like kinase (ALK)-6, is a type I serine/threonine kinase required for the signal transduction of the TGF- β family cytokines. BMP receptors include the type I receptors, BMPR-1A and BMPR-1B (50-55 kDa), and the type II receptor BMPR-II (70-80 kDa). These receptors are also closely related to the activin receptors ACV R1 and ACV R2. Type I receptors involved in BMP signaling can independently bind the various BMP family proteins in the absence of type II receptors. Soluble BMPR-IB binds BMP-4 with high-affinity in solution and is a potent BMP-4 antagonist *in vitro*. During embryogenesis, BMPR-IB is widely expressed, but in the adult, it is found only in the brain.

Reagent

Recombinant Human Bone Morphogenetic Protein Receptor IB/Fc Chimera is supplied as approximately 100 μ g of protein lyophilized from a 0.2 μ m filtered solution in phosphate buffered saline (PBS).

Preparation Instructions

Reconstitute the contents of the vial using sterile phosphate-buffered saline (PBS) containing at least 0.1% human serum albumin or bovine serum albumin. Prepare a stock solution of no less than 50 μ g/ml.

Storage/Stability

Store at -20 °C. Upon reconstitution, store at 2 °C to 8 °C for one month. For extended storage, freeze in working aliquots. Repeated freezing and thawing is not recommended. Do not store in a frost-free freezer.

Product Profile

Recombinant Human Bone Morphogenetic Protein Receptor IB/Fc Chimera is measured by its ability to inhibit the biological activity of recombinant human BMP-4-induced alkaline phosphatase production by C2C12 cells.

The ED₅₀ for this effect is generally 0.5 to 1.5 µg/ml in the presence of 200 ng/ml of recombinant human BMP-4.

The ED₅₀ is defined as the effective concentration of growth factor that elicits a 50 % increase in cell growth in a cell based bioassay.

Purity: > 90 % as determined by SDS-PAGE, visualized by silver stain.

Endotoxin level is < 0.1 ng/µg antibody as determined by the LAL (Limulus ameobocyte lysate) method.

References

1. Ide, H., et al., Cloning of human bone morphogenetic protein type IB receptor (BMPRI-IB) and its expression in prostate cancer in comparison with other BMPRI. *Oncogene*, **14**, 1377-1382 (1997).
2. Hogan, B.L.M., Bone morphogenetic proteins - multifunctional regulators of vertebrate development. *Genes Dev.*, **10**, 1580-1594 (1996).
3. Reddi, A.H., Role of morphogenetic proteins in skeletal tissue engineering and regeneration. *Nature Biotechnol.*, **16**, 247-252 (1998).
4. Francis-West, P.H., et al., BMP/GDF-signaling interactions during synovial joint development. *Cell Tissue Res.*, **296**, 111-119 (1999).
5. Mundy, G., et al., Stimulation of bone formation *in vitro* and in rodents by statins. *Science*, **286**, 1946-1949 (1999).
6. Macias, D., et al., Regulation by members of the transforming growth factor beta superfamily of the digital and interdigital fates of the autopodial limb mesoderm. *Cell Tissue Res.*, **296**, 95-102 (1999).
7. Lecanda, F., et al., Regulation of bone matrix protein expression and induction of differentiation of human osteoblasts and human bone marrow stromal cells by bone morphogenetic protein-2. *J. Cell. Biochem.*, **67**, 386-398 (1997).
8. Dale, L., and Wardle, F.C., A gradient of BMP activity specifies dorsal-ventral fates in early *Xenopus* embryos. *Seminars Cell Dev. Biol.*, **10**, 319-326 (1999).
9. Kawabata, M., et al., Signal transduction by bone morphogenetic proteins. *Cytokine Growth Factor Rev.*, **9**, 49-61 (1998).

KAA 05/01

Sigma brand products are sold through Sigma-Aldrich, Inc.

Sigma-Aldrich, Inc. warrants that its products conform to the information contained in this and other Sigma-Aldrich publications. Purchaser must determine the suitability of the product(s) for their particular use. Additional terms and conditions may apply. Please see reverse side of the invoice or packing slip.