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Product Information

Bone Morphogenetic Protein 2, human recombinant, expressed in *E. coli*

Catalog Number **B3555**, with BSA as carrier Catalog Number **B1814**, carrier free Storage Temperature –20 °C

Synonym: BMP-2

Product Description

Bone Morphogenetic Proteins (BMPs) are members of the TGF- β superfamily of cytokines that affect bone and cartilage formation.¹⁻³ Similar to other TGF- β family proteins, BMPs are highly conserved across animal species. Human, mouse, and rat BMP-2 share ~100% amino acid sequence identity.

Mature BMPs are 30–38 kDa proteins that assume a TGF- β like cysteine knot configuration. The functional form of BMP-2 is a 26 kDa protein composed of two identical 114 amino acid polypeptide chains (monomers) linked by a single disulfide bond. Each BMP-2 monomer is expressed as the C-terminal portion of a precursor polypeptide, which also contains a 23 amino acid signal sequence for secretion and a 259 amino acid propeptide. After dimerization of this precursor, cleavage by a furin-type protease forms the mature BMP-2 dimer.

Unlike TGF-β, BMPs do not form latent complexes with their propeptide counterparts. Most BMPs are homodimers, but bioactive natural heterodimers have been reported. It has been found that lovostatin (Mevinolin, Catalog Number M2147), widely used for lowering cholesterol, also increases bone formation by turning on a gene (BMP2) that promotes local bone formation.⁴ BMPs create an environment conducive for bone marrow development by stimulating the production of specific bone matrix proteins, and altering stromal cell and osteoclast proliferation.^{5,6} In addition to stimulating ectopic bone and cartilage development, BMPs may be an important factor in the development of the viscera, with roles in cell proliferation, apoptosis, differentiation, and morphogenesis.^{1,7} BMPs also appear to be responsible for normal dorsal/ventral patterning. BMPs are found in tissues that induce bone or cartilage growth, such as demineralized bone and urinary epithelium.

It has been reported that BMP-2 inhibits estradiolinduced proliferation of human breast cancer cells.⁸ BMP-2 signaling mediates apoptosis by activation of the TAK1-p38 kinase pathway that is negatively regulated by Smad6.⁹ Cellular responses to BMP-2 are mediated by the formation of hetero-oligomeric complexes of type I and type II serine/threonine kinase receptors,¹⁰ which play significant roles in BMP binding and signaling. One BMP type II receptor and two BMP type I receptors have been identified. Both BMP type I receptors bind BMP-2 with high-affinity in the absence of BMP receptor type II.

Recombinant Bone Morphogenetic Protein 2 is produced from cDNA, encoding the mature human BMP-2 protein, expressed in *E. coli*.¹¹ The products are sterile filtered through a 0.2 μ m filter and lyophilized either with 500 μ g of BSA (Catalog Number B3555) or without any carrier protein (Catalog Number B1814).

Purity: ≥98% (SDS-PAGE)

Endotoxin level: ≤1 EU /µg protein

The biological activity of BMP-2 is measured by its ability to induce alkaline phosphatase production by ATDC5 chondrogenic cells. It can also be measured by the dose-dependent stimulation of the cytolysis of MC3T3-E1 cells.

Precautions and Disclaimer

This product is for R&D use only, not for drug, household, or other uses. Please consult the Material Safety Data Sheet for information regarding hazards and safe handling practices.

Preparation Instructions

Reconstitute the contents of the vial using water to a concentration of 0.1-1.0 mg/ml. Do not vortex. This solution can then be diluted into other aqueous buffers and stored at 2-8 °C for up to one week. For extended use, freeze in working aliquots.

Storage/Stability

The lyophilized product is best stored at -20 °C. It is stable for a few weeks at room temperature. For extended storage, freeze in working aliquots. Repeated freezing and thawing is not recommended. Do not store in a frost-free freezer.

References

- Hogan, B.L.M., Bone morphogenetic proteins multifunctional regulators of vertebrate development. Genes Dev., **10**, 1580-1594 (1996).
- Reddi, A.H., Role of morphogenetic proteins in skeletal tissue engineering and regeneration. Nature Biotechnol., 16, 247-252 (1998).
- Francis-West, P.H. et al., BMP/GDF-signaling interactions during synovial joint development. Cell Tissue Res., **296**, 111-119 (1999).
- Mundy, G. et al., Stimulation of bone formation *in vitro* and in rodents by statins. Science, **286**, 1946-1949 (1999).
- 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).

- 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).
- 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).
- 8. Ghosh-Choudurya, N. et al., Bone morphogenetic protein-2 induces cyclin kinase inhibitor p21 and hypophosphorylation of retinoblastoma protein in estradiol-treated MCF-7 human breast cancer cells. Biochem. Biophys. Acta, **497**, 186-196 (2000).
- Kimura, N. et al., BMP2-induced apoptosis is mediated by activation of the TAK1-p38 kinase pathway that is negatively regulated by Smad6. J. Biol. Chem., **275**, 17647-17652 (2000).
- Kawabata, M. et al., Signal transduction by bone morphogenetic proteins. Cytokine Growth Factor Rev., 9, 49-61 (1998).
- Wozney, J. et al., Novel regulators of bone formation: molecular clones and activities. Science, 242, 1528-1534 (1988).

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