

## Product Information

### Bone Morphogenetic Protein 4

Human, Recombinant  
Expressed in mouse NSO cells

Product Number **B 2680**

#### Product Description

Bone Morphogenetic Protein 4 (BMP-4) is produced from a DNA sequence encoding the human BMP-2 (amino acid residues 1 to 282) signal peptide and propeptide fused to the human BMP-4 (amino acid residues 293 to 408) mature subunit expressed in mouse myeloma NSO cells.<sup>1</sup> Mature human BMP-4, generated after the proteolytic removal of the signal peptide and the propeptide, is a disulfide-linked homodimeric protein consisting of two 116 amino acid residue subunits. The monomer has a calculated molecular weight of 13 kDa. Due to glycosylation, the recombinant protein migrates as an approx. 22 kDa protein under reducing conditions in SDS-PAGE. Mature human and mouse BMP-4 are 98% and 100% identical, respectively, to mature rat BMP-4 in their amino acid sequence.

Bone Morphogenetic Proteins (BMP) are members of the TGF- $\beta$  superfamily of cytokines that affect bone and cartilage formation.<sup>2-4</sup> Similar to other TGF- $\beta$  family proteins, BMPs are highly conserved across animal species. Mature BMPs are 30-38 kDa proteins that assume a TGF- $\beta$ -like cysteine knot configuration. Unlike TGF- $\beta$ , 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.<sup>5</sup> 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.<sup>6, 7</sup> 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.<sup>2, 8</sup> BMPs also appear to be responsible for normal dorsal/ventral patterning.

BMP-4 specifies the development of ventral structures (e.g., skin from ectoderm and connective tissue/blood from mesoderm). Dorsal structures (nervous system and muscle) apparently appear when BMP-4 signals are interrupted through the activities of binding proteins.<sup>9</sup> BMPs are found in tissues that induce bone or cartilage growth, such as demineralized bone and urinary epithelium.

Cellular responses to BMP-4 are mediated by the formation of hetero-oligomeric complexes of type I and type II serine/threonine kinase receptors<sup>10</sup> which play significant roles in BMP binding and signaling. Two BMP type I receptors and one BMP type II receptor have been identified. Both BMP type I receptors bind BMP-4 with high-affinity in the absence of BMP receptor type II.

#### Reagent

Recombinant Human Bone Morphogenetic Protein 4 is supplied as approximately 10  $\mu$ g of protein lyophilized from a 0.2  $\mu$ m filtered solution in 30% acetonitrile and 0.1 % trifluoroacetic acid containing 50  $\mu$ g of bovine serum albumin per 1  $\mu$ g of cytokine.

#### Reconstitution

Reconstitute the contents of the vial using sterile 4 mM HCl containing at least 0.1% human serum albumin or bovine serum albumin. Prepare a stock solution of no less than 10  $\mu$ g/ml.

#### Storage/Stability

Store at  $-20$  °C.

Upon reconstitution, store at 2-8 °C for up to 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 4 is measured by its ability to induce alkaline phosphatase production by mouse ATDC-5 chondrogenic cells.<sup>11</sup> The ED<sub>50</sub> for this effect is generally 10 to 30 ng/ml.

The ED<sub>50</sub> is defined as the effective concentration of growth factor that elicits a 50% increase in cell growth in a cell based bioassay.

Endotoxin level is < 1 EU (endotoxin units) per 1 µg of the cytokine as determined by the LAL (Limulus amoebocyte lysate) method.

### References

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