

Product Information

FIBROBLAST GROWTH FACTOR RECEPTOR 4/Fc Chimera

Human, Recombinant
Expressed in mouse NSO cells

Product Number **F 8675**

Product Description

Recombinant Fibroblast Growth Factor Receptor 4/Fc Chimera is produced from a DNA sequence encoding the extracellular domain of human FGF R4 protein and fused to the carboxy-terminal Fc region of human IgG1 by a polypeptide linker.¹ Mature human FGF R4/Fc is a disulfide-linked homodimeric protein with Leu 22 at the N-terminus. The reduced monomer has a calculated molecular mass of approximately 65 kDa. As a result of glycosylation, the recombinant protein migrates to approximately 100 to 110 kDa in SDS-PAGE.

Fibroblast growth factors (FGFs) are members of a large family of structurally related polypeptides (17 kDa to 38 kDa) that exert biological activities toward cells of mesenchymal, neuronal, and epithelial origin.^{2,3} All members of the FGF superfamily have two conserved cysteine residues and a conserved 120 amino acid core region that contains six identical, interspersed amino acids.^{4,5,6} All FGFs share 30% to 50% amino acid sequence identity. FGFs are involved in normal development, wound healing and repair, angiogenesis, a variety of neurotrophic activities. They are also involved in hematopoiesis as well as in tissue remodeling and maintenance. FGFs are potent physiological regulators of growth and differentiation for a variety of cells of mesodermal, ectodermal, and endodermal origin. They have been implicated in pathological conditions such as tumorigenesis and metastasis. To date, the FGF family consists of 23 members designated FGF-1 through FGF-23.⁶

Four distinct tyrosine kinase FGF receptors (FGFRs) from four separate genes have been identified: FGFR-1 (flg, cek-1), FGFR-2 (bek, cek-3), FGFR-3 (cek-2), and FGFR-4.^{7,8} Multiple additional variants (isoforms) arising from alternative splicing have also been reported.⁸ Ligand binding specificity, signal transduction, and membrane attachment may be modified by alternative splicings.

FGF Receptors are members of a family of type I transmembrane tyrosine kinases that mediate the biological activities of the FGFs by undergoing dimerization and autophosphorylation after ligand binding. The high affinity cell surface FGF receptors have an extracellular region containing three immunoglobulin-like domains, a transmembrane region, and a cytosolic tyrosine kinase domain activated by ligand binding. Alternative splicing of the mRNAs generates multiple forms of FGF R1, FGF R2, and FGF R3. FGF-R α and FGF-R β are splicing isoforms of FGF-R.⁹ FGF-R α has three Ig-like loops in the extracellular domain, while FGF-R β has two Ig-like loops in the extracellular domain.⁹ A major determinant of ligand binding specificity is alternative splicing in the C-terminus of Ig domain III of FGF R1-3. This splicing event is tissue-specific and is likely to regulate important signaling events across epithelial (b spliced form)/mesenchymal (c spliced form) boundaries.¹⁰

FGF receptors are widely expressed during early development. FGF R4 is expressed in kidney and retina. FGF R4 has high affinity for both acidic and basic FGFs but not for keratinocyte growth factor.¹¹ FGF-19 shows exclusive binding to FGF R4.¹² Overexpression of FGF R4 or expression of variant forms of FGF R1 or FGF R2 has been linked to human breast carcinoma.^{11,13} The gene for FGF R4 maps to chromosome region 5q33-qter.¹⁴

Reagent

Recombinant Human Fibroblast Growth Factor Receptor 4/Fc Chimera is supplied as approximately 50 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 Fibroblast Growth Factor Receptor 4/Fc Chimera is measured by its ability to inhibit human FGF acidic-dependent proliferation of NR6 mouse fibroblasts.

The ED₅₀ for this effect is typically 2 to 6 ng/ml.

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 protein as determined by the LAL (Limulus amoebocyte lysate) method.

References

1. Partanen, J., et al., Proc. Natl. Acad. Sci. USA, **87**, 8913 (1990).
2. Givol, D., and Yayon, A., FASEB. J., **6**, 3362 (1992).
3. Baird, A., et al., Curr. Opin. Neurobiol., **4**, 78 (1994).
4. Fernig, F.G., and Gallagher, J.T., Prog. Growth Factor Res., **5**, 353 (1994).
5. Kirkoshi, J., et al., Biochem. Biophys. Res. Commun., **274**, 337 (2000).
6. Nishimura, T., et al., Biochem. Biophys. Acta., **1492**, 203 (2000).
7. Bernard, O., and Matthew, P., Guidebook to Cytokines and Their Receptors, Oxford Press (New York, NY: 1994).
8. Galzie, Z., et al., Biochem. Cell Biol., **75**, 669 (1997).
9. Hou, J., et al., J. Biol. Chem., **267**, 17804-17808 (1992).
10. Chellaiah, a., et al., J. Biol. Chem., **274**, 34785-34794 (1999).
11. Ron, F., et al., J. Biol. Chem., **268**, 5388 (1993).
12. Xie, M.H., et al., Cytokine, **11**, 729 (1999).
13. Penault-Llorca, F., et al., Int. J. Cancer, **61**, 170 (1995).
14. Armstrong, E., et al., Genes Chromosomes Cancer, **4**, 94 (1992).

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