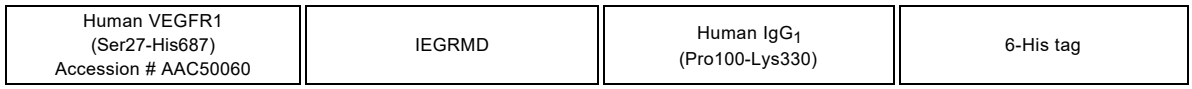
Recombinant Human VEGFR1/Flt-1 Fc Chimera

Catalog Number: 321-FL

DESCRIPTION

Source

Spodoptera frugiperda, *Sf* 21 (baculovirus)-derived human VEGFR1/Flt-1 protein



N-terminal Sequence Analysis	Ser27
Structure / Form	Disulfide-linked homodimer
Predicted Molecular Mass	100 kDa (monomer)

SPECIFICATIONS

SDS-PAGE	123 kDa, reducing conditions
Activity	Measured by its ability to inhibit the VEGF-dependent proliferation of HUVEC human umbilical vein endothelial cells. Conn, G. *et al.* (1990) Proc. Natl. Acad. Sci. USA **87**:1323. The ED_{50} for this effect is 5-30 ng/mL.
Endotoxin Level	<0.10 EU per 1 µg of the protein by the LAL method.
Purity	>90%, by SDS-PAGE visualized with Silver Staining and quantitative densitometry by Coomassie® Blue Staining.
Formulation	Lyophilized from a 0.2 µm filtered solution in MOPS, NaCl and CHAPS with BSA as a carrier protein. See Certificate of Analysis for details.

PREPARATION AND STORAGE

Reconstitution	Reconstitute at 100 µg/mL in sterile PBS containing at least 0.1% human or bovine serum albumin.
Shipping	The product is shipped at ambient temperature. Upon receipt, store it immediately at the temperature recommended below.
Stability & Storage	**Use a manual defrost freezer and avoid repeated freeze-thaw cycles.** • 12 months from date of receipt, -20 to -70 °C as supplied. • 3 months, 2 to 8 °C under sterile conditions after reconstitution.

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BACKGROUND

VEGFR1 (vascular endothelial growth factor receptor 1), also called Flt-1 (Fms-like tyrosine kinase), is a 180 kDa type I transmembrane glycoprotein in the class III subfamily of receptor tyrosine kinases (RTKs) (1, 2). While family members VEGFR1, VEGFR2/KDR/Flk-1 and VEGFR3/Flt-4 are all mainly expressed on endothelial cells and play central roles in vasculogenesis, angiogenesis, and lymphangiogenesis, only VEGFR1 is expressed on macrophages, and mainly plays inhibitory roles (1-3). VEGFR1 expression is also reported on osteoblasts, placental trophoblasts, renal mesangial cells, and some hematopoietic stem cells (1, 2). Like other class III RTKs, human VEGFR1 contains a signal peptide (aa 1-22), an extracellular domain (ECD aa 27-758) with seven Ig-like repeats, a transmembrane domain (aa 759-780) and a cytoplasmic region (aa 781-1338) with a tyrosine kinase domain and several autocatalytic phosphotyrosine sites. Human VEGFR1 ECD shares 78%, 78%, 84%, 87%, and 90% aa sequence identity with mouse, rat, porcine, canine and equine VEGFR1, respectively. Soluble forms of the VEGFR1 ECD are produced by alternative splicing, and may also be shed during regulated intracellular proteolysis (4-10). Both soluble and transmembrane forms can inhibit angiogenesis by binding and sequestering its ligands, VEGF (VEGF-A), VEGF-B or PlGF (6-11). VEGFR1 dimerizes upon ligand binding, which can include heterodimerization with VEGFR2 that modifies VEGFR2-mediated endothelial proliferation and vessel branching (8, 11, 12). VEGFR1 binds VEGF with higher affinity than does VEGFR2, but shows weaker kinase activity (9, 13). Both PlGF and VEGF induce autophosphorylation of transmembrane VEGFR1 (5, 9, 13). While deletion of mouse VEGFR1 is lethal due to overgrowth and disorganization of the vasculature, kinase-inactive mutants are viable (13, 14). VEGFR1 is up-regulated during hypoxia, and participates in neovascularization and wound healing (1, 2, 15). VEGFR1 engagement on monocyte/macrophage lineage cells enhances their migration, and release of growth factors and cytokines (1, 3, 13, 16). Lymphangiogenesis, angiogenesis, and growth-promoting effects of VEGFR1 are thought to result from enhanced migration of macrophages from the bone marrow to tumors and tissues where they recruit endothelial progenitors (3, 16). Circulating levels of VEGFR1 increase during pregnancy and are further elevated in preeclampsia (4, 6, 17).

References:

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