Recombinant Human Angiostatin Fc Chimera

Catalog Number: 926-AS

DESCRIPTION

Source Mouse myeloma cell line, NS0-derived

Met-Asp	Human IgG_1 (Pro100-Lys330)	IEGR	Human Angiostatin (Kringle 1-4) (Val98-Ala459) Accession # P00747

N-terminus C-terminus

N-terminal Sequence Analysis Met-Asp-Pro_{100}

Structure / Form Disulfide-linked homodimer

Predicted Molecular Mass 67.7 kDa (monomer)

SPECIFICATIONS

SDS-PAGE 75-85 kDa, reducing conditions

Activity Measured by the ability of the immobilized protein to support the adhesion of THP-1 human acute monocytic leukemia cells. Chavakis, T. *et al.* (2005) Blood **105**:1036.
The ED_{50} for this effect is 0.5-2.5 µg/mL.

Endotoxin Level <0.01 EU per 1 µg of the protein by the LAL method.

Purity >95%, by SDS-PAGE with silver staining, under reducing conditions.

Formulation Lyophilized from a 0.2 µm filtered solution in PBS. See Certificate of Analysis for details.

PREPARATION AND STORAGE

Reconstitution Reconstitute at 200 µg/mL in PBS.

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.
- 1 month, 2 to 8 °C under sterile conditions after reconstitution.
- 3 months, -20 to -70 °C under sterile conditions after reconstitution.

BACKGROUND

Angiostatin is an anti-angiogenic 38-45 kDa proteolytic fragment of Plasminogen, a 92-100 kDa glycosylated blood zymogen that serves as the precursor for Plasmin (1). Plasminogen is produced primarily in the liver, but also in other tissues (2). Angiostatin circulates in the plasma, binds endothelial cells and myeloid cells, is present in platelet granules, and is excreted in the urine (1, 3, 9, 10). Human Plasminogen contains an N-terminal activation peptide between amino acids (aa) 1-98, five characteristically folded kringle domains (aa 103-561), and a peptidase S1 domain (aa 581-808). Cleavage of the activation peptide produces mature Plasminogen, while further cleavage between Arg580 and Val581 by tPA (tissue plasminogen activator) produces the disulfide-linked two-subunit enzyme plasmin that dissolves fibrin clots (1, 3). Angiostatin was first identified as consisting of kringles 1-4, a form called K1-4 (1, 3, 4). Human Angiostatin (K1-4, aa 99-459) shares 79-80% aa sequence identity with mouse, rat, canine, feline, porcine and bovine K1-4. Other anti-angiogenic forms include kringles 1-3 (K1-3), or 1-4 plus most of kringle 5 (K4.5) (3, 4). K4.5, which is reported to be the most active form, occurs *in vivo* by autoproteolysis of mature Plasminogen in the presence of either a sulfhydryl donor or cell surface actin, while matrix metalloproteins such as MMP3, 7, 9 and 19 can create multiple forms (5-8). Some primary tumors promote production of Angiostatin, which paradoxically inhibits their metastatic growth (1). Angiostatin has documented anti-angiogenic and antitumor activity (3). It interferes with FGF-2 and VEGF signaling, and inhibits endothelial cell proliferation and tube formation, (1, 3, 4, 8). It also inhibits endothelial cell and macrophage migration, and up-regulates expression of anti-angiogenic thrombospondin-1 and macrophage IL-12 (3, 11-13). It promotes endothelial cell apoptosis by down-regulating Bcl-2 (3, 4, 12).

References:

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