3050 Spruce Street, St. Louis, MO 63103 USA
Tel: (800) 521-8956 (314) 771-5765 Fax: (800) 325-5052 (314) 771-5757
email: techservice@sial.com sigma-aldrich.com

Product Information

Angiostatin K1-3, human
recombinant, expressed in *Pichia pastoris*

Catalog Number **A1477**
Storage Temperature –70 °C

Synonym: K1-3

Product Description
Angiogenesis, the sprouting of new capillary growth from pre-existing blood vessels, is a multistep process.[1] Much of the increased research interest in angiogenesis is due to its role in pathological states. Angiogenesis is a rate-limiting step in tumor growth. Avascular tumors are limited in size by the diffusion distance of oxygen, nutrients, and cellular waste through the interstitium (100–200 μm). Although tumors often initially co-opt the existing vasculature, an angiogenic switch, i.e., the production of factors that induce angiogenic sprouting of the vasculature, is a necessary part of the phenotype of a successful tumor.

Under normal conditions, there is a balance between endogenous angiogenic inducers and endogenous angiogenic inhibitors that keeps the angiogenic process in check and prevents inappropriate vascularization of tissues. Endogenous inhibitors could influence one or several steps of angiogenesis. They may inhibit the expression or activity of angiogenic growth factor or inhibit the activation of proteases that prepare the extracellular matrix for vascularization. Alternatively, they may exhibit celluar processes such as endothelial cell proliferation or migration, or microtube formation. While some inhibitors display their biological effects on a variety of cell types, others specifically inhibit the growing population of endothelial cells in new blood vessels. Angiogenesis inhibitors are often derived from circulating extracellular matrix proteins, e.g., fibronectin, prolactin, collagen XVIII (endostatin), hepatocyte growth factor fragment NK1,[2-5] and angiostatin. Virtually all endogenous angiogenesis inhibitors suppress tumor growth in animal models.[6] This finding further validates the idea that tumor growth is angiogenesis dependent. Many angiogenesis inhibitors suppress both primary and metastatic tumor growth and induce tumor dormancy.[7-9] Angiostatin was the first example of an endogenous inhibitor isolated from the serum and urine of tumor-bearing animals.[10] Other inhibitors, including endostatin, TSP-1, and serpin antithrombin, have subsequently been purified from the body fluids of tumor-bearing animals.[4,11,12]

Angiostatin is an amino-terminal fragment of plasminogen that contains the first three or four kringle (K) domains.[13] Agents containing K1-3,[14] K1-4,[13] K1-5,[15] and K1-4 plus a fragment of K5[16] show potent antiangiogenic and/or antitumor growth activity. These fragments, as well as the individual kringle modules, are also inhibitory toward endothelial cell migration and/or proliferation *in vitro*. Studies with recombinant angiostatin show the tumor inhibitory activity resides in a fragment of K1-3.[17] X-ray crystallography indicates the K1-3 forms a central cavity that may contain a protein recognition site essential for their angiostatic activity.[18]

This product is a 36.4 kDa recombinant protein expressed in *Pichia pastoris*, without N-linked glycosylation. It is supplied as a frozen solution in 0.15 M sodium chloride. When thawed it will appear as a clear colorless to slightly pink solution.

Purity: ≥90% (SDS-PAGE)

Endotoxin: ≤0.50 EU/mg
(limulus amebocyte lysate [LAL] method)

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
All handling should be done under sterile conditions. Thaw the sample at room temperature with as little agitation as possible. Swirl gently to mix. After the first thaw, prepare aliquots appropriate for daily usage and store these aliquots at –70 °C until needed. Avoid freeze-thaw.

Storage/Stability
Angiostatin K1-3 should be stored at –70 °C.

References

1. Folkman, J., and Shing, Y., *J. Biol. Chem*. **267**, 10931–10934 (1992),
2. Carmeliet, P., and Jain, R.K., *Nature*, **407**, 249–257 (2000).
3. Hanahan, D., and Folkman, J., *Cell*, **86**, 353-364 (1996).
4. O′Reilly, M.S., *et al*., *Cell*, **88**, 277-285 (1997).
5. Hohenester, E., *et al*., *EMBO J*., **17**, 1656-1664 (1998).
6. Cao, Y., Haematologica, **84**, 643-650 (1999).
7. Holmgren, L., *et al*., Nat. Med., **1**, 149-153 (1995).
8. O′Reilly, M.S., *et al*., *Nat. Med*., **2**, 689-692 (1996).
9. Boehm, T., *et al*., *Nature,* **390**, 404-407 (1997).
10. O′Reilly, M.S., *et al*., *Cell*, **79**, 315-328 (1994).
11. Volpert, O.V., *et al*., *Proc. Natl. Acad. Sci. USA*, **95**, 6343-6348 (1998).
12. O′Reilly, M.S., *et al*., Science, **285**, 1926-1928 (1999).
13. Cao, Y.H., *et al*., .*J. Biol. Chem*., **271**, 29461-29467 (1996).
14. Joe, Y.A., *et al*., *Int. J. Cancer*, **82**, 694-699 (1999).
15. Cao, R.H., *et al*., *Proc. Natl Acad. Sci. USA*, **96**, 5728-5733 (1999).
16. Gately, S., *et al*., *Proc. Natl Acad. Sci. USA*, **94**, 10868-10872 (1997).
17. MacDonald, N.J., *et al*., Biochem. Biophys. Res. Commun., **264**, 469-477 (1999).
18. Marta, C. *et al*., *J. Mol. Biol*., **318**, 1009-1017 (2002).

Sold under license from CMCC.

FF,AH,RS,PHC,MAM 01/11-2