

Product Information

Endostatin, human recombinant, expressed in *Pichia pastoris*

Catalog Number **E8154**
Storage Temperature $-70\text{ }^{\circ}\text{C}$

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 development. 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 angiogenic inhibitors that keeps the angiogenic process in check and prevents inappropriate vascularization of tissues. Endogenous inhibitors could influence one or several steps in the angiogenic pathway. They may block the induction of angiogenesis by growth factors, the activity of angiogenic proteinases, endothelial cell proliferation, endothelial cell migration, or microtube formation. Endogenous angiogenesis inhibitors are often derived from blood 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 hypothesis 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 in serum and urine of tumor-bearing animals in association with tumor growth.¹⁰ Using similar approaches, endostatin, TSP-1, and the serpin antithrombin were also purified from the body fluids of tumor-bearing animals.^{4,11,12}

Endostatin (20–22 kDa) is a cleaved product of the carboxyl-terminal domain of collagen XVIII.^{13,14} It was originally found in the conditioned medium from a murine endothelial tumor cell line, hemangio-endothelioma.^{15,16} Endostatin inhibits endothelial cell migration *in vivo* and *in vitro*, and induces endothelial cell apoptosis.¹⁶ It inhibits tumor growth and impairs blood vessel maturation in wound healing.¹³ Endostatin has an important role in endothelial cell adhesion and cytoskeletal organization.¹⁷ Endostatin can be found in vessel walls (elastic fibers) and basement membranes.^{15,18} Recombinant Endostatin expressed in yeast causes G₁ arrest of endothelial cells, and endostatin treatment results in apoptosis of HUVE and HMVE cells.¹⁹

This product is an ~20 kDa recombinant protein expressed in *Pichia pastoris*. It is supplied as a frozen solution in 17 mM citrate-phosphate buffer, pH 6.2.

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 out sample at room temperature with as little agitation as possible. Swirl gently to mix. Aliquot into the appropriate amounts required for daily assays. Store these aliquots at $-70\text{ }^{\circ}\text{C}$ until needed. Avoid freeze-thaw.

Storage/Stability

Storage at $-70\text{ }^{\circ}\text{C}$ is recommended.

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. Bloch, W. *et al.*, *FASEB J.*, **14**, 2373-2376 (2000).
14. Sasaki, T. *et al.*, *J. Mol. Biol.*, **301**, 1179-1190 (2000).
15. Zatterstrom, U.K. *et al.*, *Cell Struct. Funct.*, **25**, 97-101 (2000).
16. O'Reilly, M.S. *et al.*, *Cell*, **88**, 277-285 (1997).
17. Dixelius, J. *et al.*, *Cancer Res.*, **62**, 1944-1947 (2002).
18. Miosge, M. *et al.*, *FASEB J.*, **13**, 1743-1750 (1999).
19. Dhanabal, M. *et al.*, *Biochem. Biophys. Res. Commun.*, **258**, 345-52 (1999).

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