

Product Information

Tissue Inhibitor of Metalloproteinase-2, human recombinant, expressed in CHO cells

Catalog Number **T1077**

Storage Temperature $-20\text{ }^{\circ}\text{C}$

Synonym: TIMP-2

Product Description

The tissue inhibitors of metalloproteinases (TIMPs) are naturally-occurring proteins that specifically inhibit matrix metalloproteinases (MMPs), and regulate extracellular matrix turnover and tissue remodeling by forming tightly bound inhibitory complexes with the MMPs. Thus, TIMPs maintain the balance between matrix destruction and formation. An imbalance between MMPs and the associated TIMPs may play a significant role in the invasive phenotype of malignant tumors.

TIMP proteins share several structural features including six loops held in place by six disulfide bonds arranged in three knotlike structures. The 12 cysteine residues that form these six disulfide bonds are located in conserved regions of the molecule and are essential for the formation of native conformations. The N-terminal region is necessary for inhibitory activities and contains a consensus sequence (VIRAK). Each TIMP is translated with a 29 amino acid leader sequence that is cleaved to produce the mature protein. The C-terminal regions are divergent, which may enhance the selectivity of inhibition and binding efficiency. Although the TIMP proteins share high homology, they may either be secreted extracellularly in soluble form (TIMP-1, TIMP-2, and TIMP-4) or bind to extracellular matrix components (TIMP-3).

The MMPs and TIMPs can be divided into two groups with respect to gene expression: the majority exhibit inducible expression, and a small number are produced constitutively or are expressed at very low levels and are not inducible. Among agents that induce MMP and TIMP production are the inflammatory cytokines TNF- α and IL-1 β . A marked cell type specificity is a hallmark of both MMP and TIMP gene expression (i.e., only a limited number of cell types can be induced to make these proteins).

Tissue Inhibitor of Metalloproteinase-2 (TIMP-2) was first described in 1989.^{2,4} TIMP-2 shows 40% amino acid identity with TIMP-1.² It inhibits the active form of MMP-2 and also complexes with the proform of MMP-2.^{2,4}

Like MMP-2, TIMP-2 shows little inducibility and its message levels are unaffected by TGF- β , IL-1, or TNF- α . TIMP-2, an efficient inhibitor of MMP-2, is required at low concentrations for the activation of MMP-2. It is thought that MMP-2 is activated by a membrane-bound MMP and that TIMP-2 is required to bring the MMP-2 to the cell surface. TIMP-2 is constitutively produced and secreted in a soluble form by most cell types, with major sites in the lung and liver.

This recombinant, human Tissue Inhibitor of Metalloproteinase-2 (TIMP-2) product is from a DNA sequence encoding the mature human TIMP-2 protein sequence¹ expressed in CHO cells. It can be used as a positive control in enzymatic and other assays. The 194 amino acid residue recombinant protein has a predicted molecular mass of ~22 kDa. By SDS-PAGE, the apparent molecular mass is ~20 kDa.

The product is lyophilized from a 0.2 μm filtered solution of 25 mM Tris, pH 7.5, with 150 mM sodium chloride.

The biological activity is measured by its ability to inhibit human MMP-2 hydrolysis of a peptide substrate (7-methoxycoumarin-4-yl)acetyl-Pro-Leu-Gly-Leu-(3-[2,4-dinitrophenyl]-L-2,3-diaminopropionyl)-Ala-Arg-NH₂. Recombinant human TIMP-2 has an IC₅₀ value of ~2.2 nM under conditions in which MMP-2 is present at 2.8 nM and the substrate concentration is ~5 μM .

Purity: >95% (SDS-PAGE, visualized by silver stain)

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

Add 0.1 mL of a buffer solution containing 50 mM Tris, pH 7.5, with 5 mM calcium chloride, 100 mM sodium chloride, and 0.05% BRIJ® 35, to be give a stock solution at 0.1 mg/mL.

Storage/Stability

The protein is shipped ambient and storage at -20 °C to -70 °C in a manual defrost freezer is recommended.

Upon reconstitution, this protein should be stored under sterile conditions at -20 °C to -70 °C in a manual defrost freezer. Avoid repeated freeze-thaw cycles.

References

1. Stetler-Stevenson, W.G. et al., Tissue inhibitor of metalloproteinases-2 (TIMP-2) mRNA expression in tumor cell lines and human tumor tissues. *J. Biol. Chem.*, **265**, 13933-13938 (1990).
2. Stetler-Stevenson, W.G. et al., Tissue inhibitor of metalloproteinase (TIMP-2). A new member of the metalloproteinase inhibitor family. *J. Biol. Chem.*, **264**, 17374 (1989).
3. DeClerck, Y.A. et al., Purification and characterization of two related but distinct metalloproteinase inhibitors secreted by bovine aortic endothelial cells. *J. Biol. Chem.*, **264**, 17445-17453 (1989).
4. Goldberg, G.I. et al., Human 72-kilodalton type IV collagenase forms a complex with a tissue inhibitor of metalloproteases designated TIMP-2. *Proc. Natl. Acad. Sci., USA*, **86**, 8207-8211 (1989).

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