Biodiagnostika
Oligonukleotide
Markierte Biomoleküle
BIOTEZ

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Membrane-type 1 Matrix Metalloproteinase (MT1-MMP, MMP 14) prodomain, catalytic domain, and hemopexin domain, His-tagged

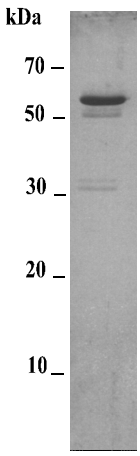
Catalogue Number: 30 100 122 Package Size: 10 µg / 50 µl
Catalogue Number: 30 100 123 Package Size: 200 µg / 1 ml

1. Enzyme characteristics

1.1 Molecular form: Recombinant soluble pro-MT1-MMP is produced as a periplasmic protein in *E. coli.* The proenzyme consists of amino acid residues Ser1 . . . Val_{501} of human MT1-MMP followed by one Thr-residue and six His-residues. The protein thus contains prodomain, catalytic domain and hemopexin domain of MT1-MMP. The calculated M_r of recombinant soluble pro-MT1-MMP is 58 200 Da.

1.2 Purity: Recombinant pro-MT1-MMP is solubilized in 50 mM Tris-HCl, pH 7.5, 150 mM NaCl, 5 mM $CaCl_2$. The protein appears as a predominant band at 58 kDa in SDS-PAGE (> 80 % of total protein).

1.3 Stability and storage: Recombinant pro-MT1-MMP is stable until the expiry date given on the label if stored at -70°C. The proenzyme can be kept at -20°C for several weeks. Repeated freezing and thawing should be avoided.



SDS-PAGE of 2 µg recombinant soluble MT1-MMP

2. Applications

Recombinant soluble pro-MT1-MMP is used as antigen for antibody generation and as antigen standard in immunoassays. The proenzyme can be activated with trace amounts of MT1-MMP catalytic domain [1, 2]. Active soluble MT1-MMP is used to study the activation of progelatinase A (matrix metalloproteinase 2) and the degradation of proteins of the extracellular matrix, including fibrillar collagens [1]. Interactions with matrix metalloproteinase inhibitors can also be investigated.

3. Introduction to structure and function of membrane-type 1 matrix metalloproteinase

Matrix metalloproteinases (MMPs) are Zn^{2+}- and Ca^{2+}-dependent endopeptidases which function in the turnover of extracellular matrix components [3]. Presently fifteen secreted MMPs and six membrane-type MMPs are known to be expressed in humans. MT1-MMP consists of 559 amino acid residues with a calculated M_r of 63 516 Da [4, 5]. The following domains and sequence regions are distinguished in MT1-MMP: Prodomain (Ser_1 - Arg_{88}), catalytic domain (Tyr_{89} - Gly_{261}), junction between catalytic domain and hemopexin domain (Gly_{262} - Gly_{292}), hemopexin-like domain (Pro_{293} - Cys_{485}) and C-terminal sequence (Pro_{486} - Val_{559}) with transmembrane segment. A soluble form of MT1-MMP without transmembrane segment has been found in culture medium of a breast carcinoma cell line [6].

MT1-MMP is expressed in adult lung, placenta, kidney, ovaries, intestine, prostate and spleen [5]. Increased amounts of the enzyme are found in tumor tissues as lung carcinoma, gastric carcinoma [7], colon, breast, head and neck carcinoma [8].

MT1-MMP is activated by removal of its prodomain. The reaction is catalyzed by furin, a subtilysin-type serine protease, which recognizes a motif of four basic amino acid residues located between prodomain and catalytic domain [9].

BioTeZ Berlin-Buch GmbH
Robert-Rössle-Str. 10, 13125 Berlin, Germany
Tel.: (0)30 / 9489-2130 Fax: (0)30 / 949-4509

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MT1-MMP activates progelatinase A (72-kDa type IV procollagenase) [4, 10, 11] and procollagenase-3 [12] by proteolytic cleavage of their prodomains. The ability of MT1-MMP to activate other matrix metalloproteinases provides potential for enhanced pericellular proteolysis in physiological and pathological processes. In particular, activation of progelatinase A by MT1-MMP is considered to contribute to local degradation of extracellular matrix during cell migration and proliferation. MT1-MMP hydrolyzes also fibrillar collagens I, II and III into characteristic ¾ and ¼ fragments [1,13] and it cleaves a number of other proteins of the extracellular matrix, among them fibronectin, vitronectin, laminin-1 and dermatan sulfate proteoglycan [1,9,13]. The activity of MT1-MMP is poorly inhibited by tissue inhibitor of matrix metalloproteinases-1 (TIMP-1), but efficiently inhibited by TIMP-2 and TIMP-3 [11].

4. References

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