

Product Information

Anti-Matrix Metalloproteinase-21, N-Terminal

Developed in Rabbit
Affinity Isolated Antibody

Product Number **M 8567**

Product Description

Anti-Matrix Metalloproteinase-21 (MMP-21), N-Terminal is developed in rabbit using a synthetic peptide corresponding to the aminoterminal end of active human matrix metalloproteinase-21 (MMP-21) as immunogen. Affinity isolated antigen specific antibody is obtained from rabbit anti-MMP-21 antiserum by immuno-specific purification which removes essentially all rabbit serum proteins, including immunoglobulins, which do not specifically bind to the peptide.

Anti-Matrix Metalloproteinase-21, active form may be used for the detection and localization of matrix metalloproteinase-21. The antibody recognizes the neoepitope formed when MMP-21 is enzymatically activated. By immunoblotting against the reduced protein, the antibody identifies bands at 70 kDa and 66 kDa. This is larger than the predicted 65 kDa and possibly represents alternative splicing, post-translational modifications, aggregation, or other phenomenon. The antibody specifically binds to MMP-21 and does not cross react with the other MMP family members (MMP-1, MMP-2, MMP-3, MMP-9, etc.).

The matrix metalloproteinases (MMPs) are a family of at least eighteen secreted and membrane-bound zinc-endopeptidases. Collectively, these enzymes can degrade all the components of the extracellular matrix, including fibrillar and non-fibrillar collagens, fibronectin, laminin and basement membrane glycoproteins. In general, a signal peptide, a propeptide, and a catalytic domain containing the highly conserved zinc-binding site characterizes the structure of the MMPs. In addition, fibronectin-like repeats, a hinge region, and a C-terminal hemopexin-like domain allow categorization of MMPs into the collagenase, gelatinase, stromelysin and membrane-type MMP subfamilies.¹⁻³ MMPs contain the motif His-Glu-X-X-His (X represents any amino acid) that binds zinc in the catalytic site, as well as another zinc molecule and two calcium molecules

structurally. They fall within the matrixin subfamily and are EC designated 3.4.24.x. This group also contains astacin, repprolysin, and serralysin, as well as other more divergent metalloproteinases. All MMPs are synthesized as proenzymes, and most of them are secreted from the cells as proenzymes. Thus, the activation of these proenzymes is a critical step that leads to extracellular matrix breakdown.

MMPs are considered to play an important role in wound healing, apoptosis, bone elongation, embryo development, uterine involution, angiogenesis,⁴ and tissue remodeling, and in diseases such as multiple sclerosis,^{2,5} Alzheimer's,² malignant gliomas,² lupus, arthritis, periodontitis, glomerulonephritis, atherosclerosis, tissue ulceration, and in cancer cell invasion and metastasis.⁶ Numerous studies have shown that there is a close association between expression of various members of the MMP family by tumors and their proliferative and invasive behavior and metastatic potential.

The tissue inhibitors of metalloproteinases (TIMPs) are naturally occurring proteins that specifically inhibit matrix metalloproteinases and regulate extracellular matrix turnover and tissue remodeling by forming tight-binding 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. 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., a limited number of cell types can be induced to make these proteins).

Matrix Metalloproteinase-21 was first cloned from *Xenopus* embryos and named XMMP.⁷ Although human MMP-21 is 77% and 68% identical to mouse and rat MMP-21 respectively, it is only 57% identical to *Xenopus* XMMP, and 29% identical with the closest human MMP, MMP-19.⁷⁻⁹ Later XMMP was given the moniker MMP-21. *Xenopus* MMP-21 compares most closely to human MMP-19, and along with MMP-22 shares an inserted cysteine residue in the catalytic domain relative to the other MMPs.⁸ Human MMP-21 encodes a 569 amino acid protein with a predicted molecular weight of approximately 65 kDa. The signal sequence and lack of a transmembrane domain leads to the assumption that MMP-21 is a secreted MMP. Unlike most other MMPs, MMP-21 contains a proline-rich, vitronectin-like insert following the cysteine switch. Phylogenetically, MMP-21 may be one of the earliest MMPs.⁸ MMP-21 also has the shortest hinge region of the MMPs. It also contains a furin cleavage motif, suggesting activation by prohormone convertases. MMP-21 appears to be restricted to embryonic stages of development in normal tissues, but is also expressed by some cancer cell lines.¹⁰

MMP-21 digests casein and gelatin poorly. The substrate specificity is not yet known. Regulation of MMP-21 may be through the Wnt pathway, which is much different than the other MMPs.¹¹

Reagent

Anti-Matrix Metalloproteinase-21, N-Terminal is supplied in phosphate buffered saline containing 50% glycerol and 0.05% sodium azide. The protein concentration is approximately 1 mg/ml.

Precautions and Disclaimer

Due to the sodium azide content a material safety data sheet (MSDS) for this product has been sent to the attention of the safety officer of your institution. Consult the MSDS for information regarding hazards and safe handling practices.

Storage/Stability

For continuous use, store at 2-8 °C for up to six months. For extended storage, the solution may be stored -20 °C. Do not store below -22 °C. If slight turbidity occurs upon prolonged storage, clarify the solution by centrifugation before use.

Product Profile

A minimum working antibody dilution of 1:1,000 is determined by immunoblotting a tissue cell lysate with an alkaline phosphatase conjugated secondary antibody and BCIP/NBT as the substrate. A starting dilution of 1:5,000 of anti-MMP-21 is recommended for chemiluminescent substrates.

Note: Higher antibody dilutions may be necessary for non-human samples.

In order to obtain the best results and assay sensitivity in various techniques and preparations, we recommend determining the optimum working dilution by titration.

References

1. Borkakoti, N., Matrix metalloproteinases: variations on a theme. *Prog. Biophys. Mol. Biol.*, **70**, 73-94 (1998).
2. Yong, V.W., et al., Matrix metalloproteinases and diseases of the CNS. *Trends in Neuroscience*, **21**, 75-80 (1998).
3. Kähäri, V.M., and Saarialho-Kere, U., Matrix metalloproteinases in skin. *Exp. Dermatol.*, **6**, 199-213 (1997).
4. Parks, W.C., and Mecham, R.P., Matrix metalloproteinases. Academic Press (1998).
5. Chandler, S., et al., Matrix metalloproteinases, tumor necrosis factor, and multiple sclerosis: an overview. *J. Neuroimmunol.*, **72**, 155-161 (1997).
6. Birkedal-Hansen, H., et al., Matrix metalloproteinases: a review. *Crit. Rev. Oral. Biol. Med.*, **4**, 197-250 (1993).
7. Yang, M., et al., A novel matrix metalloproteinase gene (XMMP) encoding vitronectin-like motifs is transiently expressed in *Xenopus laevis* early embryo development. *J. Biol. Chem.*, **272**, 13527-13533 (1997).
8. Yang, M., and Kurkinen, M., Cloning and characterization of a novel matrix metalloproteinase (MMP), CMMP, from chicken embryo fibroblasts. CMMP, *Xenopus* XMMP, and human MMP19 have a conserved unique cysteine in the catalytic domain. *J. Biol. Chem.*, **273**, 17893-17900 (1998).
9. Suzuki, A.S., et al., Expression of a novel matrix Metalloproteinase gene during *Cynops* early embryogenesis. *Biochem. Biophys. Res. Commun.*, **288**, 380-384 (2001).

10. Ahokas, K., et al., Matrix metalloproteinase-21, the human orthologues for XMMP, is expressed during fetal development and in cancer. *Gene*, **301**, 31-41 (2002).
11. Marchenko, G.N., et al., The structure and regulation of the human and mouse matrix metalloproteinase-21 gene and protein. *Biochem. J.*, **372**, 503-515 (2003).

kaa/jpa 06/03

Sigma brand products are sold through Sigma-Aldrich, Inc.

Sigma-Aldrich, Inc. warrants that its products conform to the information contained in this and other Sigma-Aldrich publications. Purchaser must determine the suitability of the product(s) for their particular use. Additional terms and conditions may apply. Please see reverse side of the invoice or packing slip.