

ProductInformation

ANTI-MATRIX METALLOPROTEINASE-18 (MMP-18), HINGE REGION

Developed in Rabbit, Affinity Isolated Antibody

Product Number **M5059**

Product Description

Anti-Matrix Metalloproteinase-18 (MMP-18) is developed in rabbit using a synthetic peptide corresponding to the hinge region of *Xenopus* MMP-18 (collagenase-4, *Xenopus* collagenase) as immunogen. Affinity isolated antigen specific antibody is obtained from rabbit anti-MMP-18 antiserum by immuno-specific purification which removes essentially all rabbit serum proteins, including immunoglobulins, which do not specifically bind to the peptide.

Rabbit Anti-MMP-18, Hinge Region may be used for the detection and localization of *Xenopus* MMP-18 by various immunochemical techniques including immunoblotting, immunoprecipitation, immunohistochemistry, and ELISA.

Rabbit Anti-MMP-18, Hinge Region specifically binds to MMP-18 and does not cross-react with the other MMP family members (MMP-1, MMP-2, MMP-3, MMP-9, etc). The antibody recognizes the pro-form and active forms of MMP-18, as well as further activation/breakdown products. By immunoblotting against the reduced protein, the antibody reacts with bands at 53 kDa and 51 kDa, as well as the smaller activated forms. Anti-MMP-18, hinge region also recognizes non-reduced MMP-18.

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, stomelysin 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, replotysin, 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-18 (MMP-18), also known as collagenase-4 and *Xenopus* collagenase, is an interstitial collagenase. This protein was originally described in *Xenopus* during early development.⁷ *Xenopus* collagenase (MMP-18) has no sequence homology with any of the other known collagenases and is distinct from MMP-1, which it most closely resembles. This protein digests intact type-I collagen at the same site as the classical collagenases (MMP-1, MMP-8, and MMP-13).

Xenopus collagenase may facilitate larval tissue degeneration and adult organogenesis during amphibian metamorphosis.⁸ MMP-18 (*Xenopus* collagenase) is regulated in a tissue-dependent manner. During metamorphosis, MMP-18 is transiently produced in the gastrula stage, expressed in the neurula stage, and down-regulated in the pre-tail bud stage of embryo development.⁷

Reagent

Rabbit Anti-MMP-18, Hinge Region is supplied in 0.01 M phosphate buffered saline, pH 7.4, containing 50 % glycerol and 0.1 % sodium azide. 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 °C to 8 °C for up to six months. For extended storage, the solution may be stored 0 °C to -20 °C. The antibody is supplied with 50 % glycerol to prevent freezing. If slight turbidity occurs upon prolonged storage, clarify the solution by centrifugation before use.

Product Profile

A working dilution of 1:1,000 is determined by immunoblotting using an alkaline phosphatase

conjugated secondary antibody and BCIP/NBT as the substrate.

Note: MMP-18 is produced at very low levels in normal, quiescent *Xenopus* cells and tissues. Collagenase production can be stimulated by mitogens such as TPA or TNF- α in receptive cell lines.

In order to obtain best results and assay sensitivity in different techniques and preparations we recommend determining optimum working dilutions by titration assay.

References

1. Borkakoti, N., Matrix metalloproteases: 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. Halpert, I., et al., Matrilysin is expressed by lipid-laden macrophages at sites of potential rupture in atherosclerotic lesions and localizes to areas of versican deposition, a proteoglycan substrate for the enzyme. *Proc. Natl. Acad. Sci., USA*, **93**, 9748-9753 (1996).
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. Stolow, M.A., et al., Identification and characterization of a novel collagenase in *Xenopus laevis*: possible roles during frog development. *Mol. Biol. Cell*, **7**, 1471-1483 (1996).

kaa 10/00

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.