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ProductInformation

ANTI-MATRIX METALLOPROTEINASE-19 (MMP-19), C-TERMINAL
Developed in Rabbit, Affinity Isolated Antibody

Product Number **M5309**

Product Description

Anti-Matrix Metalloproteinase-19 (MMP-19) is developed in rabbit using a synthetic peptide corresponding to the C-terminal of human MMP-19 (RASI-1) as immunogen. Affinity isolated antigen specific antibody is obtained from rabbit anti-MMP-19 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-19, C-terminal may be used for the detection and localization of MMP-19 by various immunochemical techniques including immunoblotting, immunoprecipitation, immunohistochemistry, and ELISA.

Rabbit Anti-MMP-19, C-terminal specifically binds to MMP-19 and does not cross-react with the other MMP family members (MMP-1, MMP-2, MMP-3, MMP-9, etc). The zymogen of MMP-19 is found at 58 kDa and is activated to a 55 kDa form, a 45-47 kDa form, and then to a 28 kDa final active form. Depending on the activation method, MMP-19 can be seen as a cascade of active forms. Anti-MMP-19, C-terminal recognizes the pro-form and most active forms of MMP-19. Since the hemopexin domain is cleaved from the smallest active form of MMP-19, the antibody will not recognize this form. By immunoblotting against the reduced protein, the antibody reacts with bands at 58 kDa (zymogen), 45 kDa (active), and a series of further cleaved active forms. Anti-MMP-19, C-terminal also recognizes non-reduced MMP-19.

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, reprolysin, 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, periodontis, glumerulonephritis, 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 metastaic 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-1β. 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-19 (MMP-19), also known as RASI-1 was first described as an MMP elevated in rheumatoid arthritis[7] and later found to be produced by a wide variety of cell types under different conditions. This enzyme is involved in the degradation of the various components of the extracellular matrix (ECM) during development, hemostasis, and pathological conditions.[8] The sequence for MMP-19 contains the canonical MMP elements of a cysteine switch (PRCGL) and a HEXGH (X refers to any amino acid) catalytic zinc site, without a furin cleavage site or transmembrane domain. MMP-19 has an 8-residue acidic patch at the beginning of the hinge region which is unlike the other MMPs.

MMP-19 is expressed in a number of cell types, including dermal fibroblasts, lung fibroblasts, and many tumor cell lines. It is also found in placenta, lung, pancreas, ovary, spleen, and intestine, suggesting a specialized role in these tissues.[7] The human MMP-19 gene has the chromosomal location of 12q14, which is a unique location for most of the MMPs.[8]

Reagent
Rabbit Anti-MMP-19, C-Terminal is supplied in 0.01 M phosphate buffered saline, pH 7.4, containing 50 % glycerol and 0.1 % 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 °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 stimulated human fibroblasts, an alkaline phosphatase conjugated secondary antibody and BCIP/NBT as the substrate. Higher antibody concentrations may be necessary for non-human samples.

Note: MMP-19 is not constituitively produced by most cell types; it has been found in lung fibroblasts and gingival fibroblasts when stimulated with TPA, as well as breast tumor and osteosarcoma cell lines. Since cell types differ greatly in the quantity of MMP-19 produced, the conditioned media may require mitogen stimulation or protein concentration to visualize the bands by immunoblotting.

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. Biophy. 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 metallo-proteinases: a review. Crit. Rev. Oral. Biol. Med., **4**, 197-250 (1993).
7. Pendas, A.M., et al., Identification and character-ization of a novel human matrix metalloproteinase with unique structural characteristics, chromosomal location, and tissue distribution. J. Biol. Chem., **272**, 4281-4286 (1997).
8. Stracke, J.O., et al., Matrix metalloproteinases 19 and 20 cleave aggrecan and cartilage oligomeric matrix protein (COMP). FEBS Lett., **478**, 52-56 (2000).

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