3050 Spruce Street
Saint Louis, Missouri 63103 USA
Telephone 800-325-5832 • (314) 771-5765
Fax (314) 286-7828
email: techserv@sial.com
sigma-aldrich.com

ProductInformation

Anti-Matrix Metalloproteinase-26, Propeptide Region
Developed in Rabbit
Affinity Isolated Antibody

Product Number **M 5192**

Product Description

Anti-Matrix Metalloproteinase-26 (MMP-26), Propeptide Region is developed in rabbit using a synthetic peptide corresponding to the propeptide domain of human matrix metalloproteinase-26 (MMP-26) as immunogen. Affinity isolated antigen specific antibody is obtained from rabbit anti-MMP-26 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-26, Propeptide Region may be used for the detection and localization of human matrix metalloproteinase-26. The antibody specifically binds to MMP-26 and does not cross react with the other MMP family members (MMP-1, MMP-2, MMP-3, MMP-7, etc.). By immunoblotting against the reduced protein, the antibody identifies bands at 30 kDa (zymogen). Activated MMP-26 is not detected, since the propeptide domain is released upon activation.

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-26 (MMP-26), also known as matrilysin-2, was initially cloned from human fetal cells [7] and identified as a matrix metalloproteinase closely related to MMP-7 (matrilysin-1). The homology between MMP-7 and MMP-26 is low (only 38% identical), thus the functions are unlikely to be similar. Homology is higher (48% identical) for the comparable region of MMP-12, but MMP-26 appears to have broader substrate specificity than MMP-12. MMP-26, like MMP-7, lacks the hemopexin domain common to the other MMPs, but contains a propeptide domain, cysteine switch activation site, followed by a catalytic domain, and a short vestige of the hinge region. MMP-26 is apparently not glycosylated, and is a secreted MMP.

Tissue analysis shows MMP-26 is strongly expressed in placenta and uterus, as well as malignant tumors and tumor cell lines.[8] MMP-26 is also expressed in kidney cells, lung cells, and lymphocytes. It was found to be widely expressed in carcinoma cells of epithelial origin (lung and endometrial).[9, 10] MMP-26 is proteolytically active, cleaving casein in zymograms, and also gelatin, α1-proteinase inhibitor, fibrinogen, fibronectin, vitronectin, type IV collagen, and apparently activating MMP-9. The proteolytic activity is blocked by TIMP-1 and TIMP-2. MMP-26 has a specific functional role in tumor progression and angiogenesis.[10]

The MMP-26 gene maps to human chromosome 11p15.3.[10]

Reagent
Anti-Matrix Metalloproteinase-26, Propeptide Region is supplied in 0.01 M phosphate buffered saline, pH 7.4, 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
By immunoblotting, a minimum working antibody dilution of 1:1,000 is recommended using a cell lysate, an alkaline phosphatase conjugated secondary antibody, and BCIP/NBT as the substrate. A starting dilution of 1:5,000 of anti-MMP-26 is recommended for chemiluminescent substrates.

MMP-26 (matrilysin-2) does not appear to be produced by most normal quiescent cells, but the treatment of many cell types with the phorbol ester TPA or IL-1 stimulates production of MMP-26. Because of the low protein levels produced (pg/ml) concentration of cell culture media is often required to visualize the bands by immunoblotting.

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 optimum working dilutions by titration.

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. de Coignac, A.B., et al. Cloning of MMP-26. A novel matrilysin-like porteinase. Eur. J. Biochem., **267**, 3323-3329 (2000).
8. Uria, J.A., and Lopez-Otin, C., Matrilysin-2, a new matrix metalloproteinase expressed in human tumors and showing the minimal domain organization required for secretion, latency, and activity. Cancer Res., **60**, 4745-4751 (2000).

9. Marchenko, G.N., et al., Promoter characterization of the novel human matrix metalloproteinase-26 gene: regulation by the T-cell factor-4 implies specific expression of the gene in cancer cells of epithelial origin. Biochem. J., **363**, 253-262 (2002).

10. Marchenko, G.N., et al., Characterization of matrix metalloproteinase-26, a novel metalloproteinase widely expressed in cancer cells of epithelial origin. Biochem. J., **356**, 705-718 (2001).

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