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-11 (MMP-11), Hinge Region
Developed in Rabbit, Affinity Isolated Antibody

Product Number **M9058**

Product Description

Anti-Matrix Meltalloproteinase-11 (MMP-11) is developed in rabbit using a synthetic peptide corresponding to the hinge region of human matrix metalloproteinase-11 (stromelysin-3) as immunogen. The antibody is affinity purified using peptide agarose.

Rabbit Anti-MMP-11 specifically binds to MMP-11 and does not cross-react with other MMP family members (MMP-1, MMP-2, MMP-3, MMP-9, etc). By immunoblotting against the reduced protein, the antibody reacts with bands at 58 kD and 45 kD and a series of further cleaved active forms. It also reacts with non-reduced MMP-11. It also reacts with non-reduced MMP-11. The antibody may be used for immunoprecipitation, immunohistochemistry and ELISA.

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, the structure of MMPs is characterized by a signal peptide, a propeptide, and a catalytic domain containing the highly conserved zinc-binding site. 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.[1,2,3] MMPs contain the motif His-Glu-Xaa-His 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-11 (MMP-11, Stromelysin-3) was first cloned from breast tumors. The MMP-11 was found to be expressed by the normal cells surrounding the carcinoma, rather than the carcinoma cells.[7] MMP-11 is produced by a wide variety of cell types under different conditions. The sequence for MMP-11 is most similar to MMP-3, but MMP-11 seems to have a much more restricted substrate specificity or much lower activity than MMP-3 (stromelysin-1). In addition, MMP-11 contains a furin-cleavage site that MMP-3 lacks. MMP-11 has been detected in a number of cell types, including dermal fibroblasts, lung fibroblasts and many tumor cell lines. MMP-11 is secreted in a glycosylated

form, the zymogen is found at 64 kDa. The enzyme is activated to a 58 kDa form, a 45-47 kDa size and then a 28 kDa active form. Depending on the activation method, MMP-11 can be seen as a cascade of active forms. MMP-11 expression is stimulated by retinoic acid.[8]

The human MMP-11 gene has the chromosomal location of 22q11.2.[9]

Reagents
Rabbit Anti-MMP-11, Hinge Region is supplied in 0.01 M phosphate buffered saline, pH 7.4, containing 50% glycerol and 15 mM sodium azide as preservative. 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 one month. For extended storage, the solution may be stored at 0° to –20°C. The antibody is supplied with 50% glycerol to prevent freezing. If slight turbidity occurs upon pro-longed storage, clarify the solution by centrifugation before use.

Product Profile
A working dilution of 1:1,000 is determined by immunoblotting using a concentrated cell culture media from a stimulated human cell line, and an alkaline phosphatase conjugated secondary antibody using BCIP/NBT as substrate. Higher antibody concentrations may be necessary for non-human samples.

Note: MMP-11 is not constitutively produced by most cell types; it has been found in lung fibroblasts, and gingival fibroblasts when stimulated with EGF, as well as breast tumor and osteosarcoma cell lines. Cell types differ greatly in quantity of MMP-11 produced; the conditioned media may require 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 (1998).
2. Yong, V.W., et al., Matrix metalloproteinases and diseases of the CNS. Trends in Neuroscience, **21**, 75 (1998).
3. Kähäri, V.-M., and Saarialho-Kere, U., Matrix metalloproteinases in skin. Exp. Dermatol., **6**, 199 (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 (1996).
5. Chandler, S., et al., Matrix metalloproteinases, tumor necrosis factor and multiple sclerosis: an overview. J. Neuroimmunol., **72**, 155 (1997).
6. Birkedal-Hansen, H., et al., Matrix metalloproteinases: a review. Crit. Rev. Oral. Biol. Med., **4**, 197 (1993).
7. Basset, P., et al., A Novel Metalloproteinase gene specifically expressed in stromal cells of breast carcinomas. Nature, **348**, 699-704 (1990).
8. Guerin, E., et al., Stromelysin-3 induction and interstitial collagenase repression by retinoic acid: Therapeutic implication of receptor-selective retinoids dissociating transactivation and AP-1-mediated transrepression. J. Biol. Chem., **272**, 11088-11095 (1997).
9. Levy, A., et al., Assignment of the human stromelysin-3 gene to the q11.2 region of chromosome 22. Genomics, **13**, 881-883 (1992).

lpg 6/00