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ProductInformation

Matrix Metalloproteinase-9 from mouse, recombinant expressed in BHK cells

Catalog Number **M1552**
Storage Temperature –70 °C

EC 3.4.24.35
Synonyms: MMP-9; Gelatinase-B; 105 kDa Gelatinase

Product Description
Mouse Matrix Metalloproteinase-9 (MMP-9) is a matrix metalloproteinase that has been substrate-affinity purified from the cell culture medium of BHK (baby hamster kidney) cells transfected with mouse 105 kDa gelatinase. MMP-9 is free of its endogenous inhibitor, TIMP-1, and other matrix metalloproteinases.

Matrix Metalloproteinase-9 may be used in various immunochemical techniques such as immunoblotting, ELISA, enzyme kinetics assays, and substrate assays. By immunoblotting, a band is detected at ~105 kDa. Mouse MMP-9 (105 kDa) is slightly larger than human MMP-9 (92 kDa).

Matrix Metalloproteinase-9 (MMP-9) is predominantly in the zymogen form, with a small amount of active enzyme present. The zymogen can be activated by incubation at 37 °C for 2–6 hours with the organomercurial compound APMA at 1 mM.[1]

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.[2-4] 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.

MMPs 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,[5] and tissue remodeling, and in diseases such as multiple sclerosis,[3,6] Alzheimer's,[3] malignant gliomas,[3] lupus, arthritis, periodontis, glomerulonephritis, atherosclerosis, tissue ulceration, and in cancer cell invasion and metastasis.[7] 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-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).

Human and mouse matrix metalloproteinase-9 are both type IV collagenases that degrade a broad range of substrates including gelatin, type IV, V, and XIV collagens, α_2-macroglobulin, elastin, vitronectin, and proteoglycan. Structurally, MMP-9 is divided into five distinct domains: a pro-domain which is cleaved upon activation; a catalytic domain containing the zinc binding site, a fibronectin-like domain that has a role in substrate targeting, a collagen-like domain, and a carboxyl terminal (hemopexin-like) domain.

The expression of MMP-9 is more restricted than MMP-2. MMP-2 and MMP-9 have an important role in the final degradation of fibrillar collagens after initial cleavage by collagenases. Interestingly, both MMP-2 and MMP-9 have been reported to also possess collagenolytic activity. MMP-2 cleaves native type I collagen to N-terminal ¾ and C-terminal ¼ fragments identical to those generated by collagenases.[8] In addition, MMP-9, which is expressed specifically by osteoclasts during murine fetal development and in adult human bone, has shown to cleave type I, II, and V collagens in the N-terminal non-helical telopeptide.[9] Because of their ability to initiate and continue degradation of fibrillar collagen type I, MMP-2 and MMP-9 are thought to play a more important role in the remodeling of collagenous ECM (extracellular matrix).

In general, inducers such as PMA, EGF, IL-1β, or TNF-α enhance MMP-9 production without altering MMP-2 levels, whereas TGF-β, which down-regulates most MMPs, enhances the expression of both MMP-2 and MMP-9.[10] MMP-9 is produced by keratinocytes and PMN leukocytes. Monocytes and macrophages also produce MMP-9.

MMP-9 is constitutively produced in some tumor cell lines and transformed cells, but not in most quiescent cells and tissues. Treatment of cells with the phorbol ester TPA stimulates production of MMP-9 in some cell types, but the low protein levels produced (pg/ml) often require concentration of the cell culture medium to visualize the bands by immunoblotting. MMP-2 and MMP-9 may be enriched from conditioned cell culture media by binding to gelatin-agarose and eluting with 10% DMSO.

Reagent
The product is supplied in a phosphate buffered solution, pH 7.4, containing 250 mM sodium chloride, 0.6% (v/v) DMSO, and 50% (v/v) glycerol.

Precautions and Disclaimer
This product is for R&D use only, not for drug, household, or other uses. Please consult the Material Safety Data Sheet for information regarding hazards and safe handling practices.

Storage/Stability
The product ships on dry ice and storage at –70 °C in aliquots is recommended. Repeated freezing and thawing is not recommended nor is storage in "frost-free" freezers.

TIMP-1, an endogenous inhibitor to MMP-9, is often complexed with this enzyme *in vivo*, but it has been removed from this preparation, leaving MMP-9 relatively unstable and it must be stored carefully.

References

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