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ProductInformation

Matrix Metalloproteinase-3 from human fibroblasts

Catalog Number **M1677**
Store at –20 °C

EC 3.4.24.17

Synonyms: Stromelysin-1; Transin; Proteoglycanase; MMP-3

Product Description
Matrix Metalloproteinase-3 (MMP-3) is a matrix metalloproteinase that has been substrate-affinity purified from cell culture medium of human fibroblasts. MMP-3 is free of its endogenous inhibitors, TIMP-1 and TIMP-2, and other matrix metalloproteinases.

Matrix Metalloproteinase-3 (MMP-3) may be used as a positive control in various applications such as enzyme kinetics assays, immunoblotting, EIA, and PAGE standards, and substrate assays. This product is a mixture of the zymogen and active enzyme. The zymogen is detected as 59 kDa and 57 kDa bands, representing the glycosylated and non-glycosylated forms. The active enzyme is detected at 45 kDa and breaks down to a 28 kDa form.

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, 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-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-3 (MMP-3) degrades a wide range of substrates, including gelatin, type IV, V, IX, and X collagens, elastin, laminin, vitronectin, casein, fibronectin, proteoglycans, aggrecan, myelin basic protein, and α-1-antitrypsin.[8,9] MMP-3 can be induced by cytokines IL-1β and TNF-α, by growth factors EGF, PDGF, and IGFBP-3, and by the tumor promotor PMA.

Its expression is inhibited by TGF-β and by all-trans retinoic acid (RA). The MMP-3 substrate repertoire extends beyond the extracellular matrix proteins and suggests that MMP-3 has additional roles other than in direct tissue remodeling (i.e., enzyme cascades and cytokine regulation).

MMP-3 does not cleave the triple helical region of the interstitial collagens, which is a characteristic that distinguishes the stromelysins from the collagenases. Structurally, MMP-3 is divided into several distinct domains: a pro-domain which is cleaved upon activation, a catalytic domain containing the zinc binding site, a short hinge region, and a carboxyl terminal (hemopexin-like) domain. Keratinocytes and fibroblasts express MMP-3 (stromelysin-1) and MMP-10 (stromelysin-2). Chrondrocytes, osteoblasts, endothelial cells, smooth muscle cells, and macrophages also express MMP-3. The human MMP-3 gene has the chromosomal location of 11q22.2-22.3.

Reagent
Supplied as a solution in a buffer of 50 mM Tris, pH 7.4, containing 0.5 M sodium chloride, 10 mM calcium chloride, 0.05% Brij-35, and 0.02% sodium azide. Each vial contains ~10 µg of human MMP-3. The buffer should be exchanged before use in cell culture (e.g., via desalting spin column). Because sodium azide is toxic, it should be removed by dialysis or a spin column before using this product on cells.

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
Store at –20 °C in aliquots. Repeated freezing and thawing is not recommended. Storage in "frost-free" freezers is not recommended.

When stripped of TIMPs, MMP-3 is unstable and must be stored carefully to avoid degradation. TIMP-1 and TIMP-2, endogenous inhibitors to MMP-3, are often complexed with this enzyme *in vivo*, but they have been removed from this preparation, leaving the MMP-3 relatively unstable and requiring careful storage.

Product Profile
MMP-3 is produced by a wide variety of cells in culture at low levels, and can be induced to much higher levels by mitogens such as IL-1, TNF, and the phorbol ester, TPA. In addition, cell types differ greatly in the quantity of MMP-3 produced. MMP-3 is usually secreted with its endogenous inhibitors, TIMP-1 and TIMP-2. MMP-3 degrades a wide variety of ECM components including fibronectin, collagens I, IV, IX, and X, laminin, aggrecan core protein and cartilage link protein and others. *In vitro*, casein or transferrin are often used as substrates. Cell lines and tissue culture reagents are certified free of tested pathogens.

Purity: ≥95% pure as tested by SDS-PAGE

References

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