

MMP2 (matrix metalloproteinase 2 (gelatinase A, 72kDa gelatinase, 72kDa type IV collagenase).

Identity

Other names

CLG4 (Collagenase Type IV),

CLG4A (Collagenase Type IV-A),

TBE-1(as secreted by H-ras oncogene-transformed human bronchial epithelial cells),

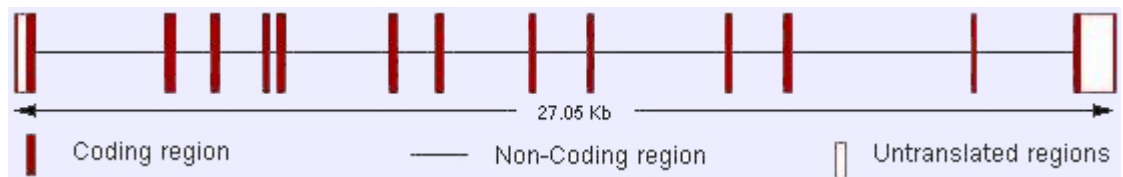
MMP-II.

Hugo

[MMP2](#)

Location 16q13-q21

DNA/RNA



Description This gene can be found on chromosome 16 at location: 54,070,604-54,097,652

Transcription The DNA sequence contains 13 exons and the transcript length: 3,069 bps translated to a 660 residues protein.

Protein



Domain structure of the MMP2.

Pre: signal sequence;

Pro: propeptide with a free zinc-ligating thiol (SH) group;

Zn: zinc-binding site;

II: collagen-binding fibronectin type II inserts;

H: hinge region;

The hemopexin/vitronectin-like domain contains four repeats with the first and last linked by a disulfide bond.

Description MMP2 is a Zn^{+2} dependent endopeptidase, synthesized and secreted in zymogen form. The nascent form of the protein shows an N-terminal

signal sequence ("pre" domain) that directs the protein to the endoplasmic reticulum. The pre domain is followed by a propeptide-"pro" domain that maintains enzyme-latency until cleaved or disrupted, and a catalytic domain that contains the conserved zinc-binding region. A hemopexin/vitronectin-like domain is also seen, that is connected to the catalytic domain by a hinge or linker region. The hemopexin domain is involved in TIMP (Tissue Inhibitors of Metallo-Proteinases) binding, the binding of certain substrates, membrane activation, and some proteolytic activities. It also shows a series of three head-to-tail cysteine-rich repeats within its catalytic domain. These inserts resemble the collagen-binding type II repeats of fibronectin and are required to bind and cleave collagen and elastin.

The regulation of MMP-2 activity occurs at many levels, of which regulation through [TIMP-2](#) and its cell surface receptor, MT1-MMP ([MMP14](#)) is critically decisive. At higher levels of TIMP-2, MT1-MMP forms a ternary complex with MMP-2 through, leaving no free MT1-MMP receptors, thereby inhibiting the activation of pro-MMP-2 by MT1-MMP. But at lower levels of TIMP-2, due to availability of free MT1-MMP, MT1-MMP mediated activation of MMP-2 is observed. Further data also indicates that expression of TIMP-2, MMP-2 and MT1-MMP (MMP-14) is co-regulated transcriptionally, demonstrating an intricate network of regulation. Pro-MMP-2 activation is also seen by complex signaling induced by ECM proteins like osteopontin, various cytokines for example IL-8 in endothelial cells and other factors.

Expression	MMP2 is tightly regulated at the transcriptional and post-transcriptional levels.
Localisation	Peri/extracellular
Function	Primary function is degradation of proteins in the extracellular matrix. It proteolytically digests gelatin (denatured collagen), and types IV, V, VII, IX and X collagen. Physiologically, MMP-2 in coordination with other MMPs, play a role in normal tissue remodeling events such as embryonic development, angiogenesis, ovulation, mammary gland involution and wound healing. MMP2 is also involved in osteoblastic bone formation and/or inhibits osteoclastic bone resorption.
Homology	Homology in amino acid sequence is seen with the other members of Metalloproteinase family especially with MMP-9 .

Mutations

Germinal	<p>A G-to-A transition in codon 101 of exon 2 of MMP2 gene was detected in a Saudi family with idiopathic multicentric osteolysis. This mutation showed a replacement of an arginine by histidine (R101H) in the prodomain, a region highly conserved across species and other members of the MMP gene family that is involved in autoproteolytic activation of MMP2.</p> <p>In a case of Winchester Syndrome, a homozygous 1210G-A transition in exon 8 of the MMP2 gene, leads to glu-to-lys (E404K) substitution in the catalytic domain of the protein. The glutamic acid at codon 404 is</p>
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believed to be essential for the peptidase activity of all metalloproteinases, as its carboxyl group catalyzes 2 proton transfers, helps stabilize the transition state, and triggers the release of the products.

Implicated in

Entity Elevated expression of MMP-2, along with MMP-9 is usually seen in invasive and highly tumorigenic cancers such as [colorectal tumors](#), gastric carcinoma, pancreatic carcinoma, [breast cancer](#), oral cancer, melanoma, [malignant gliomas](#), [Chondrosarcoma](#), gastrointestinal adenocarcinoma. Levels are also increased in malignant [astrocytomas](#), carcinomatous meningitis, and brain metastases.

Oncogenesis MMPs promote tumor progression and metastasis in invasive cancers by degradation of the ECM (ExtraCellular Matrix), which consists of two main components: Basement membranes and interstitial connective tissue. Though ECM comprises of many proteins (laminin-5, proteoglycans, entactin, osteonectin) collagen IV is the major element. MMP-2 & MMP-9 efficiently degrade collagen IV and laminin-5 thereby, assisting the metastatic cancerous cells to pass through the basement membrane. The degradation of ECM not only assists migration of metastatic cancerous cells, but also allows enhanced tumor growth by providing necessary space. Further, it is noteworthy that the ratio of active to latent form of MMP-2 increased with tumor progression in invasive cancers. MMP-2, with its family members also promotes angiogenesis (a critical process required for tumor cell survival) by degrading the vascular basement membrane and the interstitium.

Note Arthritis, Autosomal recessive osteolysis disorder, Coronary Artery disease, pulmonary-emphysema and diabetic retinopathy.

External links

	Nomenclature
Hugo	MMP2
GDB	MMP2
Entrez Gene	MMP2_4313 matrix metallopeptidase 2 (gelatinase A, 72kDa gelatinase, 72kDa type IV collagenase)

	Cards
Atlas	MMP2ID41396ch16q13
GeneCards	MMP2
Ensembl	MMP2
Genatlas	MMP2
GeneLynx	MMP2
eGenome	MMP2
euGene	4313

Genomic and cartography

GoldenPath	MMP2 - chr16:54070589-54098103 + 16q12.2 (hg18-Mar_2006)
Ensembl	MMP2 - 16q12.2 [CytoView]
NCBI	Genes Cyto Gene Seq [Map View - NCBI]
OMIM	Disease map [OMIM]
HomoloGene	MMP2

Gene and transcription

Genbank	AL542407 [ENTREZ]
Genbank	AL832088 [ENTREZ]
Genbank	BC002576 [ENTREZ]
Genbank	BQ004983 [ENTREZ]
Genbank	CR598192 [ENTREZ]
RefSeq	NM_004530 [SRS] NM_004530 [ENTREZ]
AceView	MMP2 AceView - NCBI
TRASER	MMP2 Traser - Stanford
Unigene	Hs.513617 [SRS] Hs.513617 [NCBI] HS513617 [spliceNest]

Protein : pattern, domain, 3D structure

SwissProt	P08253 [SRS] P08253 [EXPASY] P08253 [INTERPRO]
Prosite	PS00546 CYSTEINE SWITCH [SRS] PS00546 CYSTEINE SWITCH [Expasy]
Prosite	PS00023 FN2_1 [SRS] PS00023 FN2_1 [Expasy]
Prosite	PS51092 FN2_2 [SRS] PS51092 FN2_2 [Expasy]
Prosite	PS00024 HEMOPEXIN [SRS] PS00024 HEMOPEXIN [Expasy]
Prosite	PS00142 ZINC PROTEASE [SRS] PS00142 ZINC PROTEASE [Expasy]
Interpro	IPR000562 FN_type2_col_bd [SRS] IPR000562 FN_type2_col_bd [EBI]
Interpro	IPR000585 Hemopexin [SRS] IPR000585 Hemopexin [EBI]
Interpro	IPR001818 Pept_M10A_M12B [SRS] IPR001818 Pept_M10A_M12B [EBI]
Interpro	IPR006025 Pept_M_Zn_BS [SRS] IPR006025 Pept_M_Zn_BS [EBI]
Interpro	IPR006026 Peptidase_M [SRS] IPR006026 Peptidase_M [EBI]
Interpro	IPR002477 PGBD_1 [SRS] IPR002477 PGBD_1 [EBI]
Interpro	IPR009070 PGBD_like [SRS] IPR009070 PGBD_like [EBI]
CluSTr	P08253
Pfam	PF00040 fn2 [SRS] PF00040 fn2 [Sanger] pfam00040 [NCBI-CDD]
Pfam	PF00045 Hemopexin [SRS] PF00045 Hemopexin [Sanger] pfam00045 [NCBI-CDD]
Pfam	PF00413 Peptidase_M10 [SRS] PF00413 Peptidase_M10 [Sanger]

]	pfam00413	[NCBI-CDD]
Pfam		PF01471 PG binding 1	[SRS]
		PF01471 PG binding 1	[Sanger]
]	pfam01471	[NCBI-CDD]
Smart		SM00059 FN2	[EMBL]
Smart		SM00120 HX	[EMBL]
Smart		SM00235 ZnMc	[EMBL]
Prodom		PD000995 FN Type II	[INRA-Toulouse]
Prodom		P08253 MMP2 HUMAN	[Domain structure]
		P08253 MMP2 HUMAN	[sequences sharing at least 1 domain]
Blocks		P08253	
PDB		1CK7	[SRS]
		1CK7	[PdbSum]
		1CK7	[IMB]
		1CK7	[RSDB]
PDB		1CXW	[SRS]
		1CXW	[PdbSum]
		1CXW	[IMB]
		1CXW	[RSDB]
PDB		1EAK	[SRS]
		1EAK	[PdbSum]
		1EAK	[IMB]
		1EAK	[RSDB]
PDB		1GEN	[SRS]
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		1GEN	[IMB]
		1GEN	[RSDB]
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		1GXD	[RSDB]
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		1HOV	[RSDB]
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		1J7M	[RSDB]
PDB		1KS0	[SRS]
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		1KS0	[IMB]
		1KS0	[RSDB]
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		1QIB	[PdbSum]
		1QIB	[IMB]
		1QIB	[RSDB]
PDB		1RTG	[SRS]
		1RTG	[PdbSum]
		1RTG	[IMB]
		1RTG	[RSDB]
HPRD		P08253	
Protein Interaction databases			
DIP		P08253	
IntAct		P08253	
Polymorphism : SNP, mutations, diseases			
OMIM		120360;277950;605156	[map]
GENECLINICS		120360;277950;605156	
SNP		MMP2	[dbSNP-NCBI]
SNP		NM_004530	[SNP-NCI]
SNP		MMP2	[GeneSNPs - Utah]
		MMP2	[HGBASE - SRS]
HAPMAP		MMP2	[HAPMAP]
General knowledge			
Family Browser		MMP2	[UCSC Family Browser]
SOURCE		NM_004530	
SMD		Hs.513617	
SAGE		Hs.513617	
Enzyme		3.4.24.24	[Enzyme-SRS]
		3.4.24.24	[Brenda-SRS]
		3.4.24.24	[KEGG]
]	3.4.24.24	[WIT]

Amigo	peptidoglycan metabolism
Amigo	gelatinase A activity
Amigo	calcium ion binding
Amigo	extracellular matrix (sensu Metazoa)
Amigo	extracellular space
Amigo	proteolysis
Amigo	zinc ion binding
Amigo	collagen catabolism
BIOCARTA	Inhibition of Matrix Metalloproteinases [Genes]
PubGene	MMP2

Other databases

Probes

[Probe](#) [MMP2 Related clones \(RZPD - Berlin\)](#)

PubMed

[PubMed](#) [256 Pubmed reference\(s\) in LocusLink](#)

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