

Supplement Table S1: List of mammalian MMPs and their major substrates

Enzyme	MMP Number	Extracellular Matrix Substrates	Non-Matrix Substrates	Cellular Sources of MMPs(Vasculature)
Collagenases				
Collagenase 1 or Interstitial Collagenase	MMP-1	Native collagens (Type II>I>II, VII, VIII, X, and XI), Denatured Collagens (Gelatin), Elastin, Fibronectin, Laminin-5, Aggrecan, Brevican Neurocan, BM-40, Decorin, Vitronectin, Entactin/ Nidogen, Tenascin, Perlecan, Connective Tissue Growth Factor (CTGF), Link protein, Myelin basic protein, Fibrin, Fibrinogen	Pro-MMP-1, Pro-MMP-2, proMMP-9, MCP (Monocyte Chemoattractant Protein)-1, MCP-3, MCP-4, Stromal Cell Derived Factor (SDF), Pro-1L-1 β , 1L-1 β , IL-8, IGFBP-2, IGFBP-3, Pro-TNF- α , CXCL5, CXCL11 precursor, Casein, C1q, Serum amyloid A protein, α_1 -Proteinase Inhibitor, α_1 -Anti-Chymotrypsin, α_2 -Macroglobulin	VECs and Macrophages [1] [2], SMCs [3] and Lymphocytes [1], Fibroblasts [4]
Collagenase 2 or Neutrophil Collagenase	MMP-8	Native collagens (Type I>II>III, VII, and X), Gelatin, Fibronectin, Laminin Subunit Gamma-2, Entactin, Aggrecan, Tenascin, Brevican Core Protein Precursor, Myelin Basic Protein, Fibrinogen	Pro-MMP-8, MCP-1, Pro-TNF- α , IL-8, L-Selectin, IGFBP, CXCL5, CXCL10, CXCL11, Substance P, Angiotensin I, Angiotensin II, Bradykinin, Ephrin-B1, Plasmin C1-Inhibitor, α_1 -Proteinase Inhibitor, α_2 -Macroglobulin	VECs [5], VSMCs, Neutrophils and Macrophages [6], T-cells
Collagenase 3	MMP-13	Native collagens (Type II>III>I, VI, VII, IX, X, and XIV), Gelatin, Fibronectin, Laminin Subunit Gamma-2, Collagen telopeptides, SDF, Brevican, Fibrillin, Aggrecan, Perlecan, CTGF, Large Tenascin-C, Osteonectin, SPARC, Biglycan, Fibrinogen	Pro-MMP-9, Pro-MMP-13, MCP-3, SDF, Pro-TNF- α , CXCL5, Factor XII, Casein, C1q, α_1 -Anti-Chymotrypsin, α_2 -Macroglobulin	VECs and Fibroblasts [7] [8], SMCs, Macrophages [9]
Collagenase 4	MMP-18	Native collagens (Type I, II, III), Gelatin, α_1 -peptidase inhibitor		
Gelatinases				
Gelatinase A or 72-KDa Gelatinase	MMP-2	Native collagens (Type I, II, III, IV, V, VII, X, and XI), Gelatin, Elastin, Fibronectin, Entactin/Nidogen-1, Aggrecan, Decorin, Fibrillin, Fibulin 2, Laminin-5, Tenascin, SPARC, Vitronectin, Galectin-1, Galectin-3, Versican, BM-40, Brevican, Neurocan, CTGF, Chondroitin Sulfate Proteoglycan (CSPG)-4, Dystroglycan, <i>Procollagen C-proteinase enhancer-1 (PCPE-1)</i> , Link Protein, Osteonectin, Myelin Basic Protein, Biglycan, Fibrin, Fibrinogen	Pro-MMP-1, Pro-MMP-2, Pro-MMP-13, MMP-12, MCP-3, SDF, Pro-TGF- β 1, Pro-TNF- α , Pro-IL-1 β , CXCL5, IGFBP-3, IGFBP-4, IGFBP-5, IGFBP-6, 14-3-3 protein, Big endothelin-1, Cystatin C, Follistatin-like 1, Alpha-actin-2, Pregnancy zone protein, Substance P, Decorin, IGFBP, Plasminogen receptor S100A10 (p11), proEMAP/p43, FGF-R1 (fibroblast growth factor receptor 1), Macrophage Migration Inhibitory Factor (MMIF), Thrombospondin-2, Plasminogen, α_1 -Proteinase Inhibitor, α_1 -Anti-Chymotrypsin, α_2 -Macroglobulin	ECs [4] [5], PAECs, PASCs [10] [1], SMCs and Lymphocytes [1], Macrophages [11], Neutrophils, T-lymphocytes [12]
Gelatinase B or 92-KDa Gelatinase	MMP-9	Native collagens (Type I, IV, V, XI, and XIV), Gelatin, Elastin, Vitronectin, Laminin, Decorin, Fibrillin, Fibronectin, SPARC, Aggrecan, Link Protein, Galectin-1, Galectin-3, Versican, Decorin, Biglycan, Link Protein, Osteonectin, Myelin Basic Protein, Fibrin, Fibrinogen	Pro-MMP-2, Pro-MMP-9, Pro-MMP-13, MCP-3, SDF, Pro-IL-8, Pro-TNF- α , Pro-TGF- β 2, Pro-IL-1 β , Cell-surface IL-2R α , CXCL5, CXCL9, CXCL10, CXCL11, FGF-R1, CTAP-III/NAP-2, GRO α , PF-4, Integrin beta-2, IGFBP-1, IGFBP-4, Substance P, Angiotensin I, Angiotensin II, release of VEGF (substrate not known), ADAMTS-4, SERPINE2, Casein, C1q, Tissue factor pathway inhibitor (TFPI), Plasminogen, α_1 -Proteinase Inhibitor, α_2 -Macroglobulin	ECs [4], SMCs [1] [2], Macrophages [13], T-lymphocytes [12], Neutrophils [14]
Stromelysins				
Stromelysin-1	MMP-3	Non triple helical regions of native Collagens (Type III, IV, V, VII, IX, X, and XI), Gelatin, Collagen Telopeptides, Elastin, Fibronectin, Vitronectin, Laminin, Entactin/ Nidogen-1, Tenascin, SPARC, Aggrecan, Decorin, Perlecan, Versican, Fibulin, Biglycan, Link Protein, Osteonectin, Myelin Basic Protein, Fibulin-2, Fibrin, Fibrinogen	Pro-MMP-1, Pro-MMP-3, Pro-MMP-7, Pro-MMP-8, Pro-MMP-9, Pro-MMP-13, MCP-1, MCP-2, MCP-3, MCP-4, SDF, Pro-TNF- α , L-selectin, Pro-HB-EGF, Pro-IL-1 β , Perlecan, Decorin, E-cadherin, IGFBP-3, Carboxymethylated transferrin (Cm-Tf), Substance P, T-kininogen, Casein, C1q, urokinase-type Plasminogen Activator (uPA), uPAR, Osteopontin, VEGFA, PAI (Plasminogen Activator Inhibitor)-1, Plasminogen, α_2 -Antiplasmin, α_1 -Proteinase Inhibitor, α_1 -Anti-	ECs [5], SMCs [2] and Lymphocytes [1] Macrophages [9]

Stromelysin-2	MMP-10	Collagens (Type I, III, IV, and V), Gelatin, Elastin, Fibronectin, Aggrecan, Brevican Hyaluronan and Proteoglycan Link Protein 1, Proteoglycan, Link Protein, Fibrinogen	Chymotrypsin, α_2 -Macroglobulin Pro-MMP-1, Pro-MMP-7, Pro-MMP-8, Pro-MMP-9, Pro-MMP-10, Casein	ECs and Macrophages [15], SMCs [16]
Stromelysin-3	MMP-11	Gelatin, Fibronectin, Collagen Type IV, Laminin, Aggrecan	Pro-MMP-11, IGFBP-1, Casein, Cm-Tf, α -actin-2, PAI-2, α_2 -Antiplasmin, α_1 -Proteinase Inhibitor, α_2 -Macroglobulin	ECs, SMCs, and Macrophages [2], Fibroblasts, B-cells [17]
Stromelysin-4 or RASI-1	MMP-19	Native collagen Type IV, Gelatin, Laminin, Entactin/ Nidogen-1, Large Tenascin-C, Fibronectin, Aggrecan, Cartilage Oligomeric Matrix Protein (COMP), Fibrin, Fibrinogen	Pro-MMP-19, MMP-9, Casein, uPAR	Capillary EC and SMCs [18], Fibroblasts [19], PBMCs, TH1 lymphocytes [20], Monocytes [17]
Matrilysins				
Matrilysin-1 or PUMP-1	MMP-7	Non helical segments of native collagen types IV, V, IX, X, XI, Gelatin, Elastin, Fibronectin, Vitronectin, Laminin, Entactin/ Nidogen-1, Tenascin, SPARC, Aggrecan, Brevican, Galectin-3, Link Protein, Decorin, Fibulin, Versican, Osteonectin, Myelin Basic Protein, Fibrin, Fibrinogen	Pro-MMP-1, Pro-MMP-2, Pro-MMP-7, Pro-MMP-9, Pro-TNF- α , Pro- α -defensin, Cell surface bound Fas-L, CXCL9, CXCL11, IGFBP-1, IGFBP-2, IGFBP-3, β_4 -integrin, E-cadherin, Apolipoprotein A1 (Apo-A1), Apo-CII, CD95-L, Casein, Cm-Tf, Osteopontin, uPA, Plasminogen, Decorin, α_1 -Proteinase Inhibitor, α_2 -Macroglobulin	ECs [21], Macrophages [22]
Matrilysin-2 or Endometase	MMP-26	Native collagen Type IV, Gelatin, Fibronectin, Vitronectin, Fibrinogen	Pro-MMP-9, Pro-MMP26, IGFBP-1, α_1 -Proteinase Inhibitor, α_2 -Macroglobulin	ECs [23], Fibroblasts, Macrophages and PMN [24, 25], B-cells [17]
Membrane-anchored				
MT1-MMP	MMP-14	Native collagens (Type I, II and III), Gelatin, Fibronectin, Tenascin, Vitronectin, Laminin, Entactin, Galectin-3, CTGF-L, Fibrillin, Aggrecan, Perlecan, Syndecan-1, Lumican, Myelin Basic Protein, Fibrinogen	Pro-MMP-2, Pro-MMP-13, Pro-MMP-14, MMP-14, MCP-3, SDF, Cell-surface CD44, RANKL, Cell-surface tissue trans-glutaminase (tTG), Pro-TNF- α , IL-8, HB-EGF, Factor XII, Pro- α_v integrin chain, Apo-CII, Apo-E, α_1 -Proteinase Inhibitor, α_2 -Macroglobulin	Vascular ECs [26], SMCs, Macrophage [27], Fibroblasts
MT2-MMP	MMP-15	Fibronectin, Tenascin, Entactin, Laminin, Aggrecan, Perlecan, Proteoglycan, Myelin Basic Protein	Pro-MMP-2, Cell-surface bound tTG, Pro-TNF- α	Fibroblasts, Leukocytes, T lymphocytes [17]
MT3-MMP	MMP-16	Collagen Type III, Gelatin, Fibronectin, Vitronectin, Laminin, Myelin Basic Protein	Pro-MMP-2, Cell-surface bound tTG, Pro-TNF- α , Metastasis-suppressor KiSS-1	ECs [28], Leukocytes, T- lymphocytes [17]
MT4-MMP	MMP-17	Gelatin, Fibrin, Fibrinogen, Myelin Basic Protein	Pro-MMP-2, Pro-TNF- α , HB-EGF, ADAMTS4 Peptidase	ECs [28], Monocytes and B-Cells [17], Fibroblast
MT5-MMP	MMP-24	Fibronectin, Gelatin, Chondroitin Sulphate Proteoglycan, Dermatan Sulphate Proteoglycan.	Pro-MMP-2, KiSS-1	T-lymphocytes [17], Leukocytes
MT6-MMP or Leukolysin	MMP-25	Native collagen Type IV, Gelatin, Laminin-1, Fibronectin, Chondroitin Sulphate Proteoglycan, Dermatan Sulphate Proteoglycan, Myelin Basic Protein, Fibrin, Fibrinogen	Pro-MMP-2, Pro-MMP-9, uPAR α_1 -Proteinase Inhibitor	Monocytes [17], Leukocytes [29]
Other MMPs				

Macrophage Metalloelastase	MMP-12	Collagens (Type I, V, And IV), Gelatin, Elastin, Fibronectin, Vitronectin, Laminin, Entactin, Osteonectin, Decorin, Aggrecan, Biglycan, Fibrillin, Myelin Basic Protein, Fibrin, Fibrinogen	Plasminogen, Pro-TNF- α , ApoA-1, CXCL9, CXCL10, CXCL11, uPAR, vWF, Factor XII, TFPI, α_1 -Proteinase Inhibitor	SMCs [30], Macrophage [9]
Enamelysin	MMP-20	Collagen XVIII, Amelogenin, Ameloblastin, Aggrecan, Laminin, COMP	Pro-MMP-20 (autolysis)	
X-MMP (Xenopus)	MMP-21	Gelatin, Aggrecan	Casein	Fibroblasts, Macrophages [24]
C-MMP (Chicken)	MMP-22	No matrix substrates defined		
Cysteine Array MMP (CA-MMP) or Femalysin	MMP-23	Gelatin, Casein, Fibronectin		
CA-MMP (Gallus)	MMP-27	Gelatin	Pro-MMP-27 (autolysis), Casein	B-cells [17]
Epilysin (CA-MMP)	MMP-28	No matrix substrates defined	Casein	T-lymphocytes [17]

MMPs are categorized according to their substrate specificity. This extensive list of substrates represents both bona fide and potential substrate candidates. Modified from Sterlinc and Werb., 2001 [31]; Overall., 2002 [32], Visse and Nagase., 2003 [33], Nagase., 2006 [34] and *MEROPS* database (<http://merops.sanger.ac.uk>). VECs, Vascular Endothelial Cells; VSMCs, Vascular Smooth Muscle Cells;

Supplement Table S2: Selective inhibitors for MMPs

Inhibitor	MMP Number	References
ARP-100	MMP-2	Chetty C et al., 2010 [35]
<i>cis</i> -9-Octadecenoyl-N-hydroxylamide	MMP-2	Wang Z et al., 2011 [36]
UK 370106	MMP-3	Whitlock et al., 2007 [37]
AC10781F	MMP-3	Johnson LL et al., 1999 [38]
CGS 27023A	MMP-3	MacPherson LJ et al., 1997[39]
REGA-3G12 (mAb)	MMP-9	Martens E et al., 2007 [40]
AS111793	MMP-12	Quément et al., 2008 [41]
MMP408	MMP-12	Li W et al., 2009 [42]
Compound 1	MMP-13	Blagg JA et al., 2005 [43], Shah M et al., 2012 [44]
Compound 2	MMP-13	Johnson AR et al., 2007 [45]
Pyrimidine dicarboxamides	MMP-13	Engel CK et al., 2005 [46]
CL-82198	MMP-13	Wu J et al., 2005 [47]
Peptide G, PG	MT1-MMP	Suojanen J et al., 2009 [48]
DX-2400 (mAb)	MT1-MMP	Devy L et al., 2009 [49]
Piperazine 4u	MMP-9, MMP-13	Levin, JI et al. 2001 [50]
CRV and PPC Peptides	Pro-MMP-9	Suojanen J et al., 2011 [51]
<i>cis</i> -ACCP	MMP-2>MMP-9	Hoffman, A et al., 2008 [52]
CTT1, CTT2	Gelatinases (MMP-2, MMP-9)	Heikkilä P et al., 2006 [53]
N-sulfonylamino acid derivative	Gelatinases (MMP-2, MMP-9)	Tamura Y et al., 1998 [54]
SB-3CT	Gelatinases (MMP-2, MMP-9)	Kleifeld O et al., 2001 [55]
Chlorhexidine, Dihydrochloride	Gelatinases MMP-2>MMP-9, MMP-8	Gendron R et al., 1999 [56]

Abbreviation: mAb - Monoclonal Antibody

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