

Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

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Literature references

- Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics*, 18, 142. [↗](#)
- Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics*, 33, 3461-3467. [↗](#)
- Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res*, 46, D649-D655. [↗](#)
- Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology*, 14, e1005968. [↗](#)

Reactome database release: 77

This document contains 1 pathway and 34 reactions ([see Table of Contents](#))

cleavage of the major fibril forming collagens I, II and III at neutral pH, and thus thought to define the rate-limiting step in normal tissue remodeling events. All can cleave additional substrates including other collagen subtypes. Collagenases cut collagen alpha chains at a single conserved Gly-Ile/Leu site approximately 3/4 of the molecule's length from the N-terminus (Fields 1991, Chung et al. 2004). The cleavage site is characterised by the motif G(I/L)(A/L); the G-I/L bond is cleaved. In collagen type I this corresponds to G953-I954 in the Uniprot canonical alpha chain sequences (often given as G775-I776 in literature). It is not clear why only this bond is cleaved, as the motif occurs at several other places in the chain. MMP14, a membrane-associated MMP also known as Membrane-type matrix metalloproteinase 1 (MT-MMP1), is able to cleave collagen types I, II and III (Ohuchi et al. 1997).

Literature references

- Steinhusen, U., Weiske, J., Badock, V., Tauber, R., Bommert, K., Huber, O. (2001). Cleavage and shedding of E-cadherin after induction of apoptosis. *J. Biol. Chem.*, 276, 4972-80. [↗](#)
- Hadler-Olsen, E., Fadnes, B., Sylte, I., Uhlin-Hansen, L., Winberg, JO. (2011). Regulation of matrix metalloproteinase activity in health and disease. *FEBS J*, 278, 28-45. [↗](#)
- Shapiro, SD. (1998). Matrix metalloproteinase degradation of extracellular matrix: biological consequences. *Curr Opin Cell Biol*, 10, 602-8. [↗](#)

Editions

2011-07-12	Authored	Jupe, S.
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2012-11-12	Edited	Jupe, S.

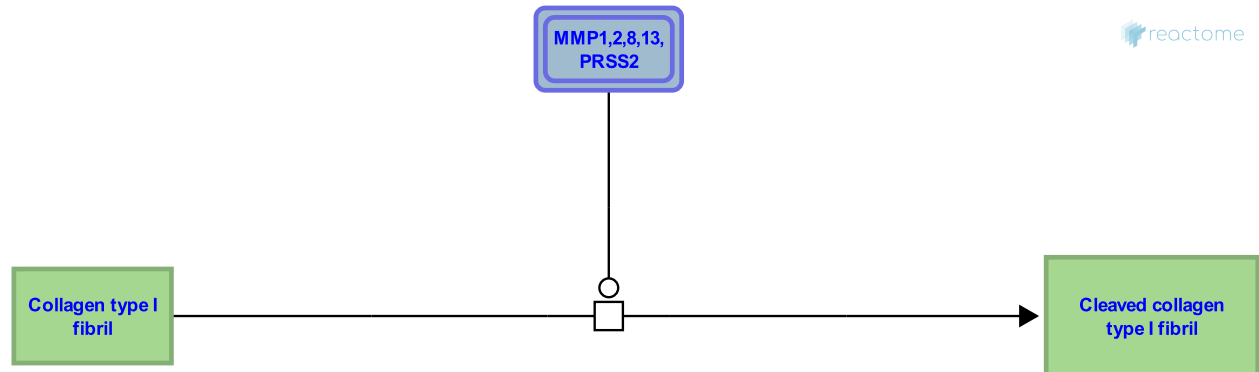
Collagen type I degradation by MMP1,2,8,13, PRSS2 ↗

Location: [Collagen degradation](#)

Stable identifier: R-HSA-1454822

Type: transition

Compartments: extracellular region



MMP1 (Welgus et al. 1981), MMP8 (Hasty et al. 1987), and MMP13 (Knauper et al. 1996) known in the literature as collagenases I, II and III respectively are able to digest the intrahelical bonds of collagen type I. MMP2, also known as Gelatinase-A, was found to cleave collagen type I fibrils (Aimes & Quigley 1995). Though this was disputed (Seltzre & Eisen 1999) there is a structural explanation for the apparent discrepancies in experimental data (Patterson et al. 2001). In addition trypsin-2 is able to degrade native soluble type I collagen (Moilanen et al. 2003).

Degradation is represented here at a theoretical end point where every alpha strand has been cleaved.

Followed by: [Gelatin degradation by MMP19](#), [Gelatin degradation by MMP1, 2, 3, 7, 8, 9, 12, 13](#)

Literature references

- Welgus, HG., Jeffrey, JJ., Eisen, AZ. (1981). The collagen substrate specificity of human skin fibroblast collagenase. *J Biol Chem*, 256, 9511-5. ↗
- Hasty, KA., Jeffrey, JJ., Hibbs, MS., Welgus, HG. (1987). The collagen substrate specificity of human neutrophil collagenase. *J Biol Chem*, 262, 10048-52. ↗
- Knäuper, V., López-Otin, C., Smith, B., Knight, G., Murphy, G. (1996). Biochemical characterization of human collagenase-3. *J Biol Chem*, 271, 1544-50. ↗
- Aimes, RT., Quigley, JP. (1995). Matrix metalloproteinase-2 is an interstitial collagenase. Inhibitor-free enzyme catalyzes the cleavage of collagen fibrils and soluble native type I collagen generating the specific 3/4- and 1/4-length fragments. *J Biol Chem*, 270, 5872-6. ↗
- Chung, L., Dinakarbandian, D., Yoshida, N., Lauer-Fields, JL., Fields, GB., Visse, R. et al. (2004). Collagenase unwinds triple-helical collagen prior to peptide bond hydrolysis. *EMBO J*, 23, 3020-30. ↗

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Collagen type I degradation by MMP14 ↗

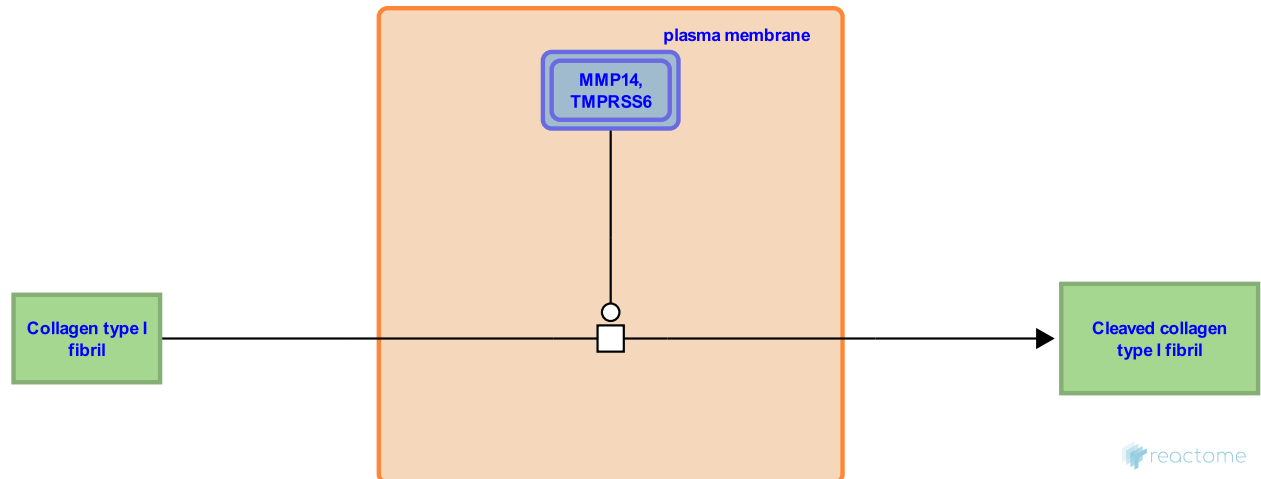
Location: [Collagen degradation](#)

Stable identifier: R-HSA-1458433

Type: transition

Compartments: plasma membrane

Inferred from: [Collagen type I degradation by MMP14 \(Cavia porcellus\)](#)



The membrane-type MMP MMP14 (MT1-MMP) is a fibrillar collagenase able to degrade collagen types I, II and III (Ohuchi et al. 1997).

Followed by: [Gelatin degradation by MMP19](#), [Gelatin degradation by MMP1, 2, 3, 7, 8, 9, 12, 13](#)

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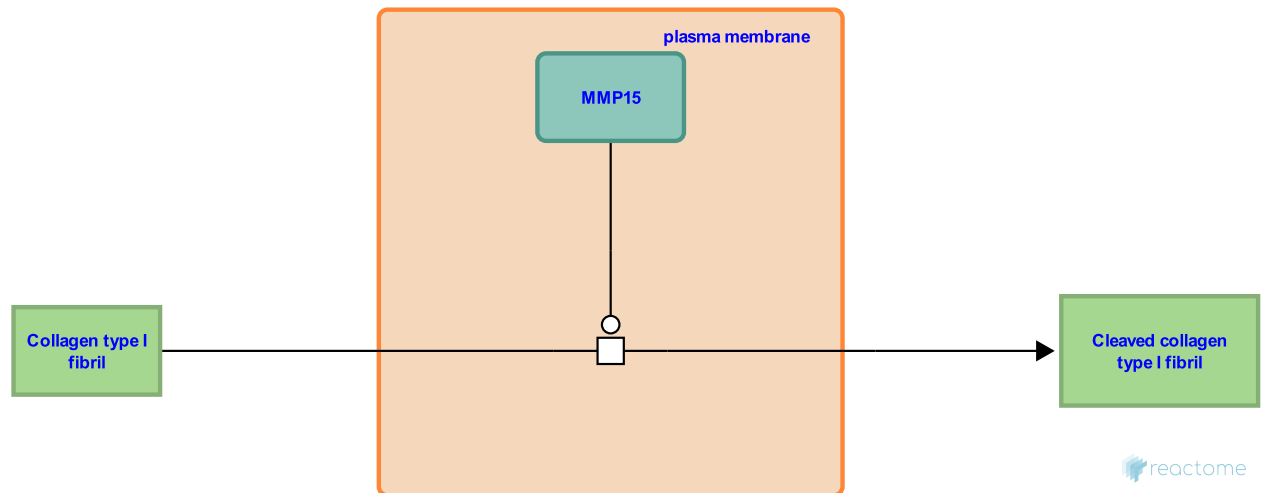
Collagen type I degradation by MMP15 ↗

Location: [Collagen degradation](#)

Stable identifier: R-HSA-2473596

Type: transition

Compartments: plasma membrane



The membrane-type MMP MMP15 (MT2-MMP) is a fibrillar collagenase able to degrade collagen type I (Morrison and Overall 2006) and believed able to degrade types II and III (Somerville et al. 2003).

Followed by: [Gelatin degradation by MMP19](#), [Gelatin degradation by MMP1, 2, 3, 7, 8, 9, 12, 13](#)

Literature references

Morrison, C.J., Overall, C.M. (2006). TIMP independence of matrix metalloproteinase (MMP)-2 activation by membrane type 2 (MT2)-MMP is determined by contributions of both the MT2-MMP catalytic and hemopexin C domains. *J Biol Chem*, 281, 26528-39. ↗

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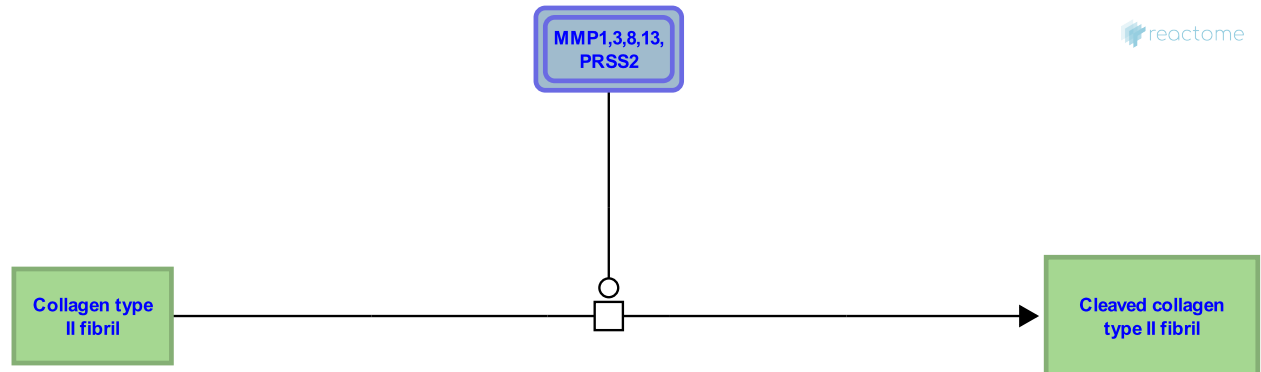
Collagen type II degradation by MMP1,3,8,13,PRSS2 ↗

Location: [Collagen degradation](#)

Stable identifier: R-HSA-1474197

Type: transition

Compartments: extracellular region



MMP1 (Welgus et al. 1981), MMP8 (Hasty et al. 1987), and MMP13 (Knauper et al. 1996, Mitchell et al. 1996, Billinghamurst et al. 1997) known in the literature as collagenases I, II and III respectively are able to digest the intrahelical bonds of collagen type II, cleaving between amino acids Gly975 and Leu976 of the Uniprot canonical sequence. Human trypsin-2 is also capable of cleaving the triple helix of human cartilage collagen type II (Stenman et al. 2005).

Followed by: [Gelatin degradation by MMP19](#), [Gelatin degradation by MMP1, 2, 3, 7, 8, 9, 12, 13](#)

Literature references

- Welgus, HG., Jeffrey, JJ., Eisen, AZ. (1981). The collagen substrate specificity of human skin fibroblast collagenase. *J Biol Chem*, 256, 9511-5. ↗
- Hasty, KA., Jeffrey, JJ., Hibbs, MS., Welgus, HG. (1987). The collagen substrate specificity of human neutrophil collagenase. *J Biol Chem*, 262, 10048-52. ↗
- Knäuper, V., López-Otin, C., Smith, B., Knight, G., Murphy, G. (1996). Biochemical characterization of human collagenase-3. *J Biol Chem*, 271, 1544-50. ↗
- Wu, JJ., Lark, MW., Chun, LE., Eyre, DR. (1991). Sites of stromelysin cleavage in collagen types II, IX, X, and XI of cartilage. *J Biol Chem*, 266, 5625-8. ↗

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Collagen type II degradation by MMP14 ↗

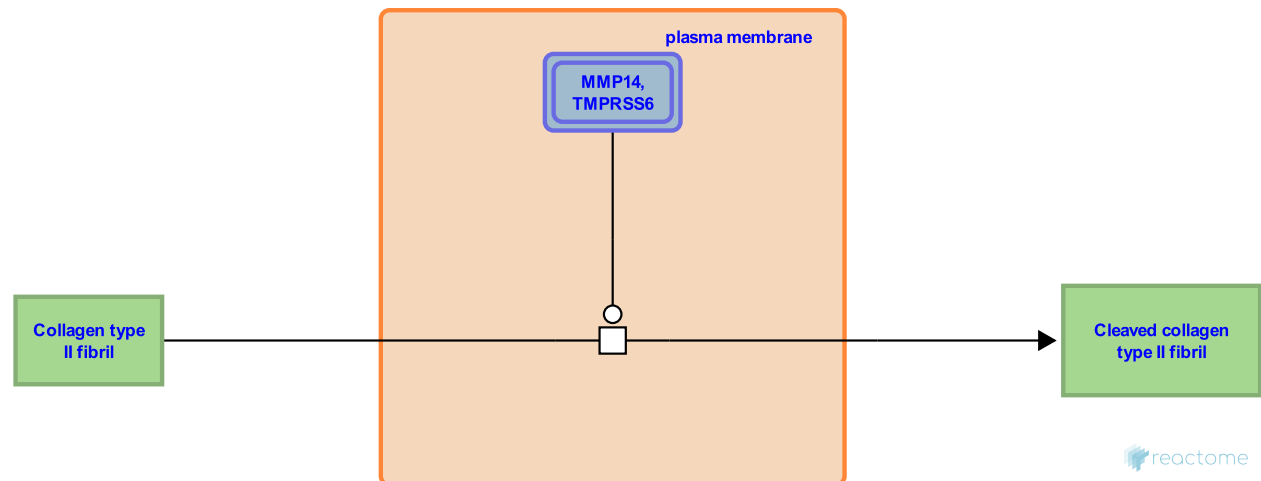
Location: [Collagen degradation](#)

Stable identifier: R-HSA-1474196

Type: transition

Compartments: plasma membrane

Inferred from: [Collagen type II degradation by MMP14 \(Homo sapiens\)](#)



The membrane-type MMP MMP14 (MT1-MMP) is a fibrillar collagenase. MMP14 is able to degrade collagen types I, II and III (Ohuchi et al. 1997).

Followed by: [Gelatin degradation by MMP19](#), [Gelatin degradation by MMP1, 2, 3, 7, 8, 9, 12, 13](#)

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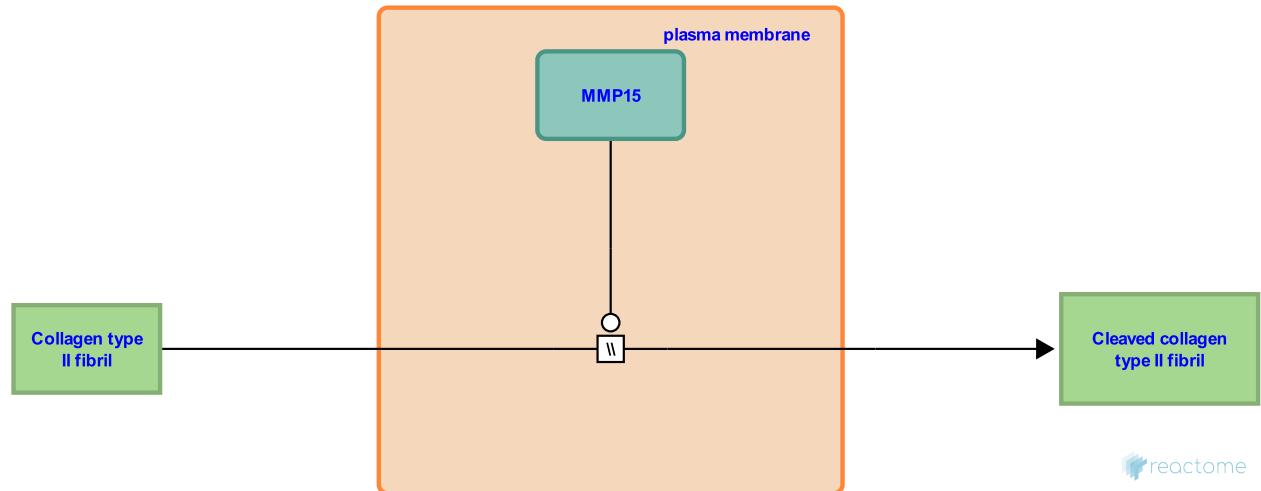
Collagen type II degradation by MMP15 ↗

Location: [Collagen degradation](#)

Stable identifier: R-HSA-2473594

Type: omitted

Compartments: plasma membrane



The membrane-type MMP MMP15 (MT2-MMP) is a fibrillar collagenase. MMP15 is able to degrade collagen type I (Morrison & Overall 2006) and believed able to degrade types II and III (Somerville et al. 2003).

Literature references

Morrison, CJ., Overall, CM. (2006). TIMP independence of matrix metalloproteinase (MMP)-2 activation by membrane type 2 (MT2)-MMP is determined by contributions of both the MT2-MMP catalytic and hemopexin C domains. *J Biol Chem*, 281, 26528-39. ↗

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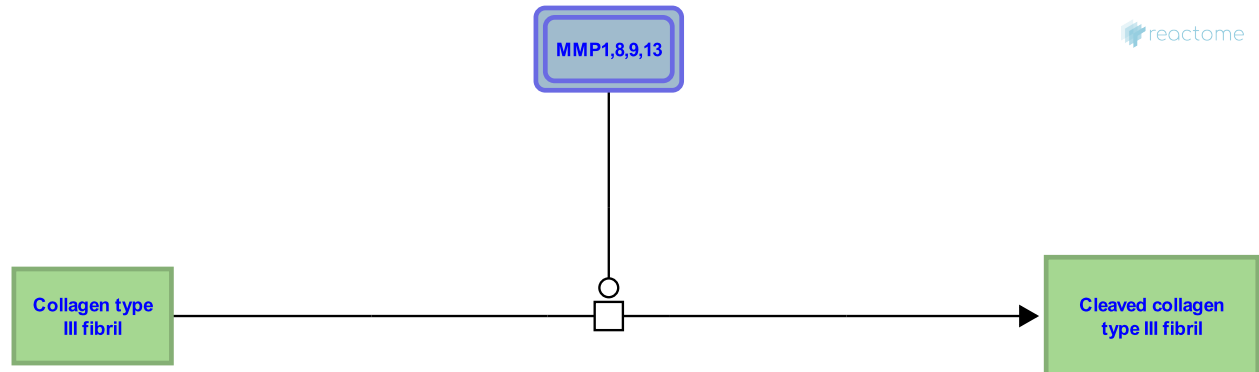
Collagen type III degradation by MMP1,8,9,13 [↗](#)

Location: [Collagen degradation](#)

Stable identifier: R-HSA-1474213

Type: transition

Compartments: extracellular region



MMP1 (Welgus et al. 1981), MMP8 (Hasty et al. 1987), and MMP13 (Knauper et al. 1996, Mitchell et al. 1996), called collagenases I, II and III respectively, are all able to cleave the intrahelical bonds of collagen type III, cleaving between amino acids Gly948 and Ile949 of the Uniprot canonical sequence. MMP9 (Bigg et al. Veidal et al. 2010) and MMP10 (Stromelysin-2) are able to degrade collagen type III (Nicholson et al. 1989).

Followed by: [Gelatin degradation by MMP19](#), [Gelatin degradation by MMP1, 2, 3, 7, 8, 9, 12, 13](#)

Literature references

- Chung, L., Dinakarbandian, D., Yoshida, N., Lauer-Fields, JL., Fields, GB., Visse, R. et al. (2004). Collagenase unwinds triple-helical collagen prior to peptide bond hydrolysis. *EMBO J*, 23, 3020-30. [↗](#)
- Welgus, HG., Jeffrey, JJ., Eisen, AZ. (1981). The collagen substrate specificity of human skin fibroblast collagenase. *J Biol Chem*, 256, 9511-5. [↗](#)
- Hasty, KA., Jeffrey, JJ., Hibbs, MS., Welgus, HG. (1987). The collagen substrate specificity of human neutrophil collagenase. *J Biol Chem*, 262, 10048-52. [↗](#)
- Knäuper, V., López-Otin, C., Smith, B., Knight, G., Murphy, G. (1996). Biochemical characterization of human collagenase-3. *J Biol Chem*, 271, 1544-50. [↗](#)
- Ohuchi, E., Imai, K., Fujii, Y., Sato, H., Seiki, M., Okada, Y. (1997). Membrane type 1 matrix metalloproteinase digests interstitial collagens and other extracellular matrix macromolecules. *J Biol Chem*, 272, 2446-51. [↗](#)

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2011-07-12	Authored	Jupe, S.
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Collagen type III degradation by MMP10 ↗

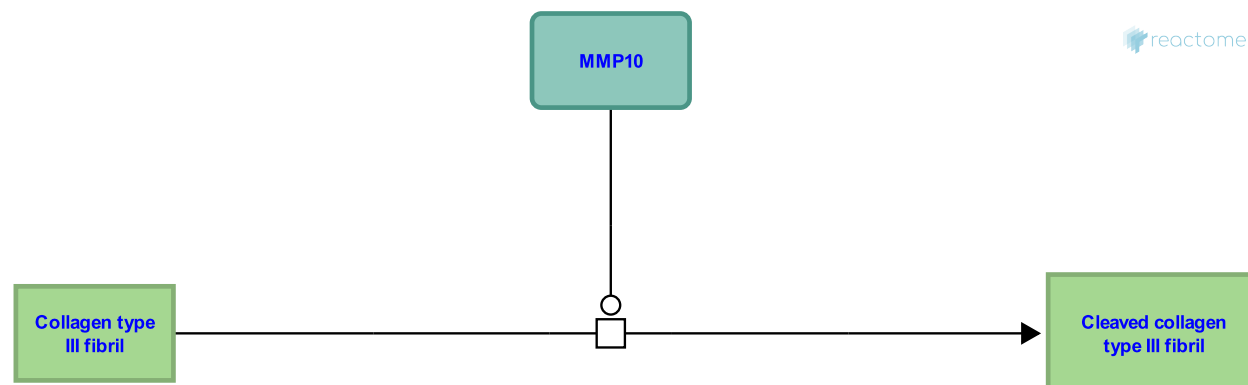
Location: [Collagen degradation](#)

Stable identifier: R-HSA-2485111

Type: transition

Compartments: extracellular region

Inferred from: [Collagen type III degradation by MMP10 \(Homo sapiens\)](#)



MMP10 (Stromelysin-2) is able to degrade collagen type III (Nicholson et al. 1989).

Followed by: [Gelatin degradation by MMP19](#), [Gelatin degradation by MMP1, 2, 3, 7, 8, 9, 12, 13](#)

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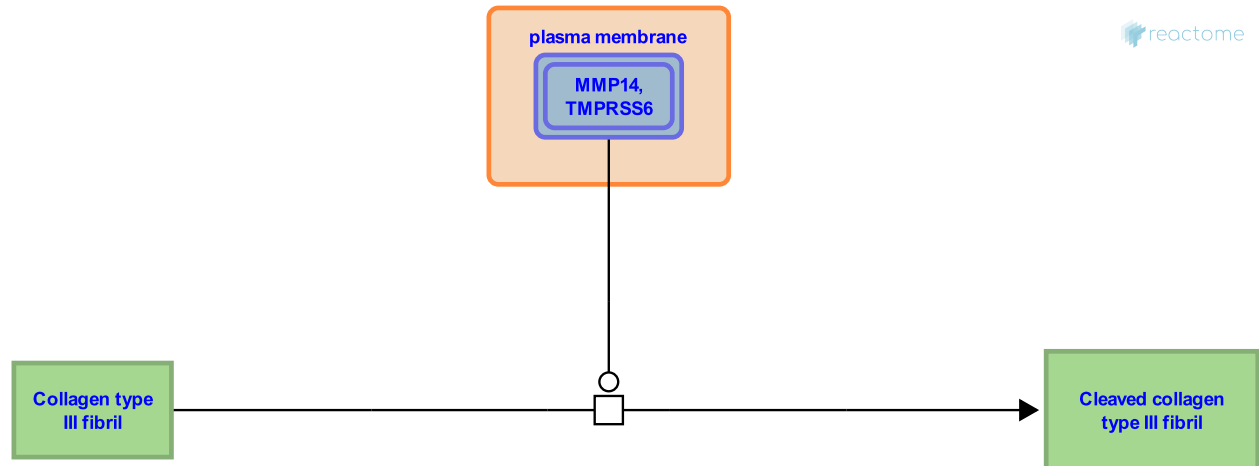
Collagen type III degradation by MMP14 [↗](#)

Location: [Collagen degradation](#)

Stable identifier: R-HSA-1474210

Type: transition

Compartments: extracellular region, plasma membrane



The membrane-type MMP MMP14 (MT1-MMP) is a fibrillar collagenase able to degrade collagen types I, II and III (Ohuchi et al. 1997).

Followed by: [Gelatin degradation by MMP19](#), [Gelatin degradation by MMP1, 2, 3, 7, 8, 9, 12, 13](#)

Literature references

Ohuchi, E., Imai, K., Fujii, Y., Sato, H., Seiki, M., Okada, Y. (1997). Membrane type 1 matrix metalloproteinase digests interstitial collagens and other extracellular matrix macromolecules. *J Biol Chem*, 272, 2446-51. [↗](#)

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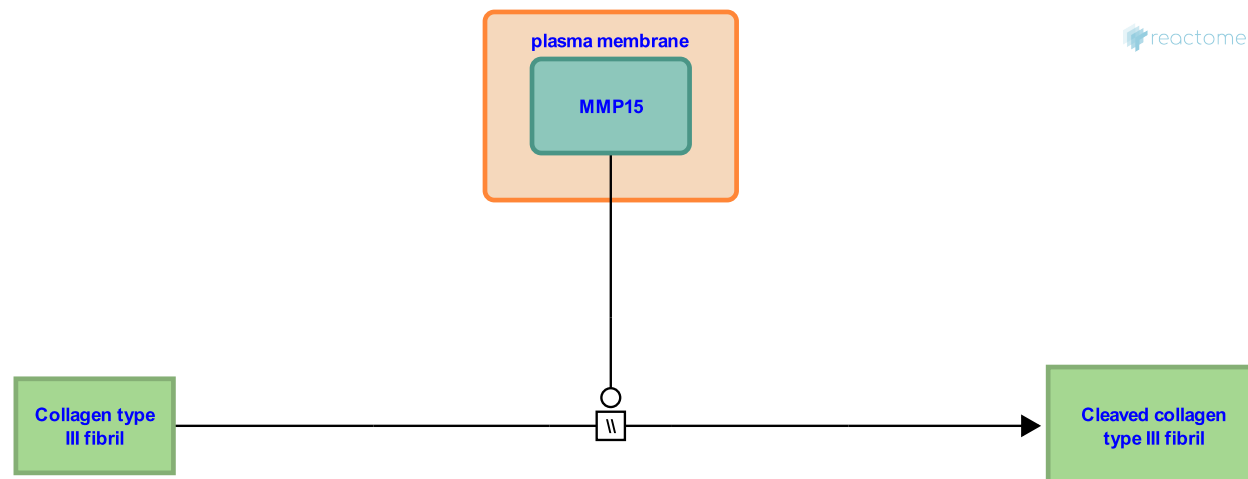
Collagen type III degradation by MMP15 [↗](#)

Location: [Collagen degradation](#)

Stable identifier: R-HSA-2473584

Type: omitted

Compartments: extracellular region, plasma membrane



The membrane-type MMP MMP15 (MT2-MMP) is a fibrillar collagenase able to degrade collagen type I (Morrison & Overall 2006) and believed able to degrade collagen types II and III (Somerville et al. 2002).

Literature references

Morrison, C.J., Overall, C.M. (2006). TIMP independence of matrix metalloproteinase (MMP)-2 activation by membrane type 2 (MT2)-MMP is determined by contributions of both the MT2-MMP catalytic and hemopexin C domains. *J Biol Chem*, 281, 26528-39. [↗](#)

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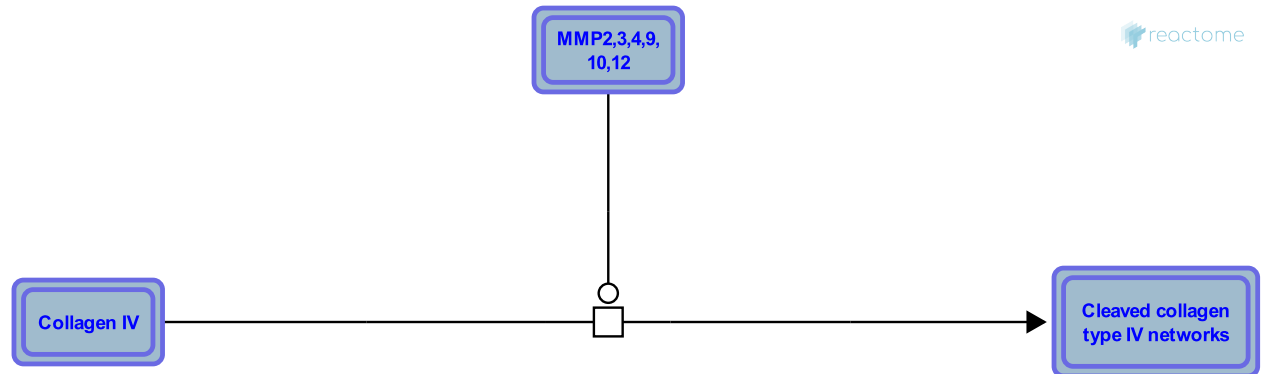
Collagen type IV degradation by MMP2,3,4,9,10,12 ↗

Location: [Collagen degradation](#)

Stable identifier: R-HSA-1564142

Type: transition

Compartments: extracellular region



Type IV collagen is the most abundant structural basement membrane (BM) component, providing a scaffold for other major BM proteins such as laminin (Charonis et al. 1985, 1986). There are six different genes encoding type IV collagen chains, alpha-1 to alpha-6(IV) with distinct tissue distributions. Three alpha chains fold to form the triple helical unit of collagen IV. Three chain combinations have been identified, alpha-1X2 alpha-2(IV), alpha-3,alpha-4, alpha-5(IV) and alpha-5X2, alpha-6(IV) (Borza et al. 2001). The first is the major form, found in all basement membranes, the other types have more restricted distributions.

Collagen IV forms a lattice network rather than extended fibrils. It can be digested by MMP2 (Liotta et al. 1981, Salo et al. 1983, Bergers et al. 2000, Monaco et al. 2006), MMP3 (Okada et al. 1986, Wilhelm et al. 1987, Bejarano et al. 1988, Nicholson et al. 1989), MMP7 (Miyazaki et al. 1990, Murphy et al. 1991), MMP9 (Moll et al. 1990, Morodomi et al. 1992, Murphy et al. 1991, Watanabe et al. 1993, Bergers et al. 2000), MMP10 (Nicholson et al. 1989) and MMP12 (Chandler et al. 1996).

Followed by: [Gelatin degradation by MMP19](#), [Gelatin degradation by MMP1, 2, 3, 7, 8, 9, 12, 13](#)

Literature references

- Liotta, LA., Tryggvason, K., Garbisa, S., Robey, PG., Abe, S. (1981). Partial purification and characterization of a neutral protease which cleaves type IV collagen. *Biochemistry*, 20, 100-4. ↗
- Monaco, S., Sparano, V., Gioia, M., Sbardella, D., Di Pierro, D., Marini, S. et al. (2006). Enzymatic processing of collagen IV by MMP-2 (gelatinase A) affects neutrophil migration and it is modulated by extracatalytic domains. *Protein Sci.*, 15, 2805-15. ↗
- Bejarano, PA., Noelken, ME., Suzuki, K., Hudson, BG., Nagase, H. (1988). Degradation of basement membranes by human matrix metalloproteinase 3 (stromelysin). *Biochem J*, 256, 413-9. ↗
- Miyazaki, K., Hattori, Y., Umenishi, F., Yasumitsu, H., Umeda, M. (1990). Purification and characterization of extracellular matrix-degrading metalloproteinase, matrin (pump-1), secreted from human rectal carcinoma cell line. *Cancer Res*, 50, 7758-64. ↗
- Moll, UM., Youngleib, GL., Rosinski, KB., Quigley, JP. (1990). Tumor promoter-stimulated Mr 92,000 gelatinase secreted by normal and malignant human cells: isolation and characterization of the enzyme from HT1080 tumor cells. *Cancer Res*, 50, 6162-70. ↗

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2011-07-12	Authored	Jupe, S.
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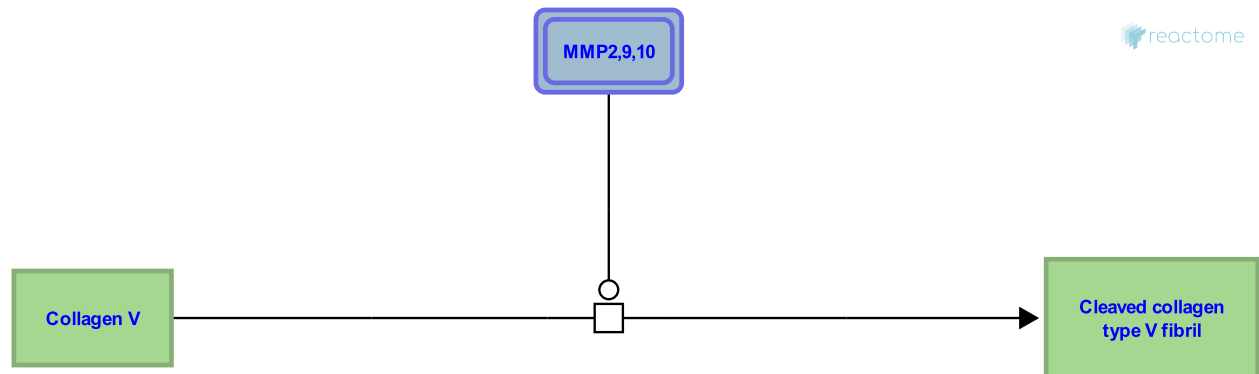
Collagen type V degradation by MMP2,9,10 [↗](#)

Location: [Collagen degradation](#)

Stable identifier: R-HSA-1564164

Type: transition

Compartments: extracellular region



Type V collagen is a fibril-forming collagen forming a group with collagen types I, II, III and XI (Gelse et al. 2003). Three different alpha chains exist that can combine in three distinct trimers. Collagen V forms fibrils that are associated with type I and to a lesser extent III collagen, as a minor but critical component of bone matrix, corneal stroma and the interstitial matrix of muscle, liver, lung and placenta (Birk et al. 1988). COL5A1^{-/-} mice have an almost complete lack of collagen fibrils reflecting a central role in fibrillogenesis (Wenstrup et al. 2004). Type V collagen mutation results in a range of connective tissue diseases including Ehlers-Danlos syndrome (EDS), which is a heterogeneous group of disorders characterized by joint hypermobility and skin hyperextensibility, thinness and fragility. These result from mutations in the COL5A1 and COL5A2 genes (Michalickova et al. 1998, Schwarze et al. 2000).

Type V collagen is digested by MMP2 (Murphy et al. 1981, Veidal et al. 2011), MMP10 (Nicholson et al. 1989), and MMP9 (Murphy et al. 1982, Watanabe et al. 1993, Pourmotabbed et al. 1994, Niyibizi et al. 1994, Veidal et al. 2011).

Followed by: [Gelatin degradation by MMP19](#), [Gelatin degradation by MMP1, 2, 3, 7, 8, 9, 12, 13](#)

Literature references

Veidal, SS., Larsen, DV., Chen, X., Sun, S., Zheng, Q., Bay-Jensen, AC. et al. (2012). MMP mediated type V collagen degradation (C5M) is elevated in ankylosing spondylitis. *Clin Biochem.* [↗](#)

Nicholson, R., Murphy, G., Breathnach, R. (1989). Human and rat malignant-tumor-associated mRNAs encode stromelysin-like metalloproteinases. *Biochemistry*, 28, 5195-203. [↗](#)

Editions

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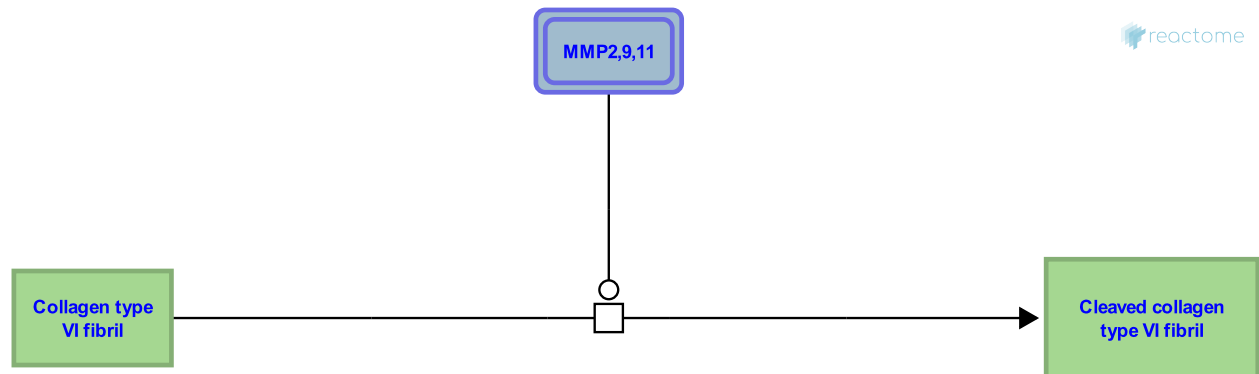
Collagen type VI degradation by MMP2,9,11 [↗](#)

Location: [Collagen degradation](#)

Stable identifier: R-HSA-1564112

Type: transition

Compartments: extracellular region



Type VI collagen aggregates into distinctive microfibrils known as beaded filaments that form an independent microfibrillar network in virtually all connective tissues except for bone (von der Mark et al. 1984). It plays a role in the maintenance of tissue integrity since it participates in both cell-matrix and matrix-matrix interactions, interacting with many other ECM proteins including fibronectin (Chang et al. 1997), type IV collagen (Kuo et al. 1997), type II collagen, decorin and biglycan (Bidanset et al. 1992). Collagen type VI has been described as a connecting protein (Gelse et al. 2003).

Collagen type VI is resistant to digestion by many MMPs but is cleaved by MMP2 (Myint et al. 1996, Veidal et al. 2011), MMP9 (Veidal et al. 2011) and MMP11 (Motrescu et al. 2008).

Followed by: [Gelatin degradation by MMP19](#), [Gelatin degradation by MMP1, 2, 3, 7, 8, 9, 12, 13](#)

Literature references

Veidal, SS., Karsdal, MA., Vassiliadis, E., Nawrocki, A., Larsen, MR., Nguyen, QH. et al. (2011). MMP mediated degradation of type VI collagen is highly associated with liver fibrosis--identification and validation of a novel biochemical marker assay. *PLoS One*, 6, e24753. [↗](#)

Motrescu, ER., Blaise, S., Etique, N., Messaddeq, N., Chenard, MP., Stoll, I. et al. (2008). Matrix metalloproteinase-11/stromelysin-3 exhibits collagenolytic function against collagen VI under normal and malignant conditions. *Oncogene*, 27, 6347-55. [↗](#)

Editions

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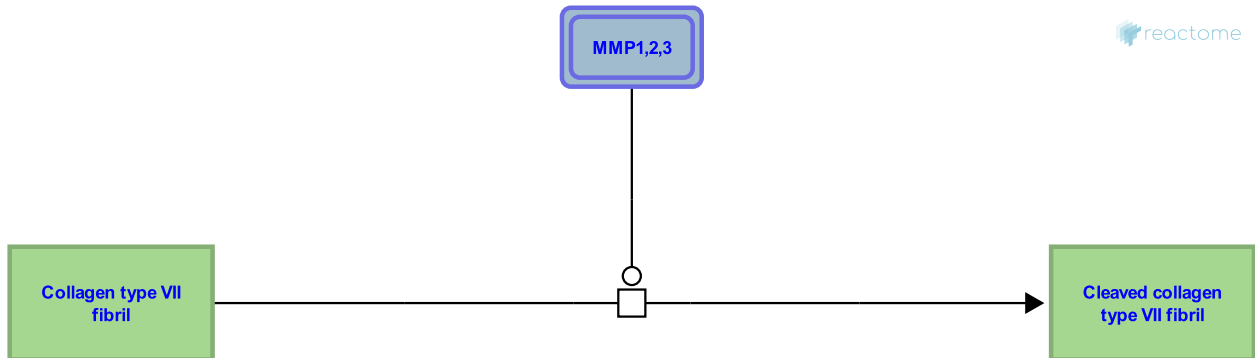
Collagen type VII degradation by MMP1,2,3 [↗](#)

Location: [Collagen degradation](#)

Stable identifier: R-HSA-1564120

Type: transition

Compartments: extracellular region



Type VII collagen is the major collagen component of anchoring fibrils, which are essential for the attachment of the epidermis to the dermis. It is degraded by MMP1 (Seltzer et al. 1989), MMP2 (Seltzer et al. 1989, Sawamura et al. 1991, Karelina et al. 2000) and MMP3 (Sawamura et al. 1991). MMP2 is 3000-fold more active than MMP1 (Seltzer et al. 1989).

Followed by: [Gelatin degradation by MMP19](#), [Gelatin degradation by MMP1, 2, 3, 7, 8, 9, 12, 13](#)

Literature references

Seltzer, JL., Eisen, AZ., Bauer, EA., Morris, NP., Glanville, RW., Burgeson, RE. (1989). Cleavage of type VII collagen by interstitial collagenase and type IV collagenase (gelatinase) derived from human skin. *J Biol Chem*, 264, 3822-6. [↗](#)

Sawamura, D., Sugawara, T., Hashimoto, I., Bruckner-Tuderman, L., Fujimoto, D., Okada, Y. et al. (1991). Increased gene expression of matrix metalloproteinase-3 (stromelysin) in skin fibroblasts from patients with severe recessive dystrophic epidermolysis bullosa. *Biochem Biophys Res Commun*, 174, 1003-8. [↗](#)

Editions

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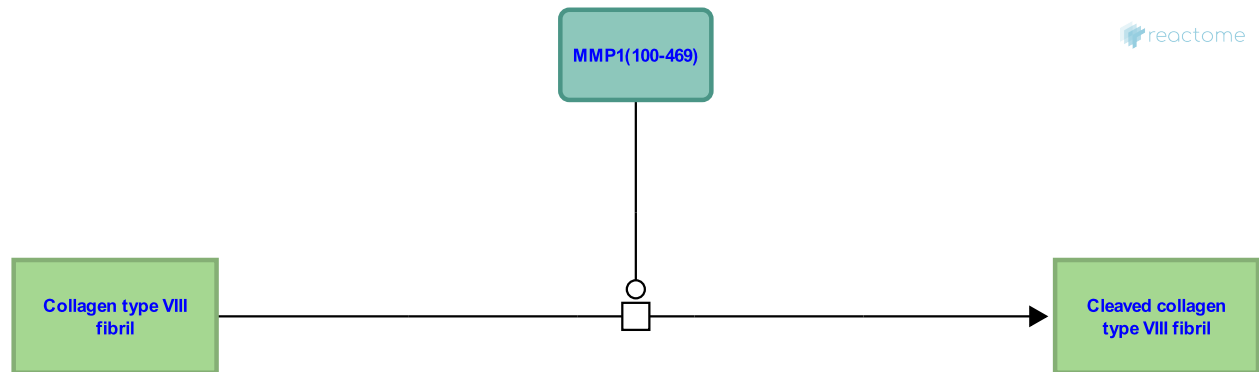
Collagen type VIII degradation by MMP1 [↗](#)

Location: [Collagen degradation](#)

Stable identifier: R-HSA-1564169

Type: transition

Compartments: extracellular region



Collagen type VIII is a short chain, network-forming collagen, thought to play a role in tissue remodeling and repair (Shuttleworth 1997, Weitkamp et al. 1999). There are two alpha chain subtypes, found in a ratio of two alpha-1 to one alpha-2 chains (Mann et al. 1990) in the typical collagen heterotrimer. Studies suggest that type VIII collagen is a major component of the hexagonal lattice seen in Descemet's membrane (Mann et al. 1990). Mutations in both alpha chains have been associated with Fuchs endothelial corneal dystrophy (FECD), a degenerative disease of the corneal endothelium (Jun et al. 2012).

Collagen type VIII can be degraded by MMP1 (Sage et al. 1983, 1984).

Followed by: [Gelatin degradation by MMP19](#), [Gelatin degradation by MMP1, 2, 3, 7, 8, 9, 12, 13](#)

Literature references

Sage, H., Balian, G., Vogel, AM., Bornstein, P. (1984). Type VIII collagen. Synthesis by normal and malignant cells in culture. *Lab Invest*, 50, 219-31. [↗](#)

Editions

2011-07-12	Authored	Jupe, S.
2012-10-08	Reviewed	Sorsa, T.
2012-11-12	Edited	Jupe, S.

Collagen type VIII degradation by ELANE ↗

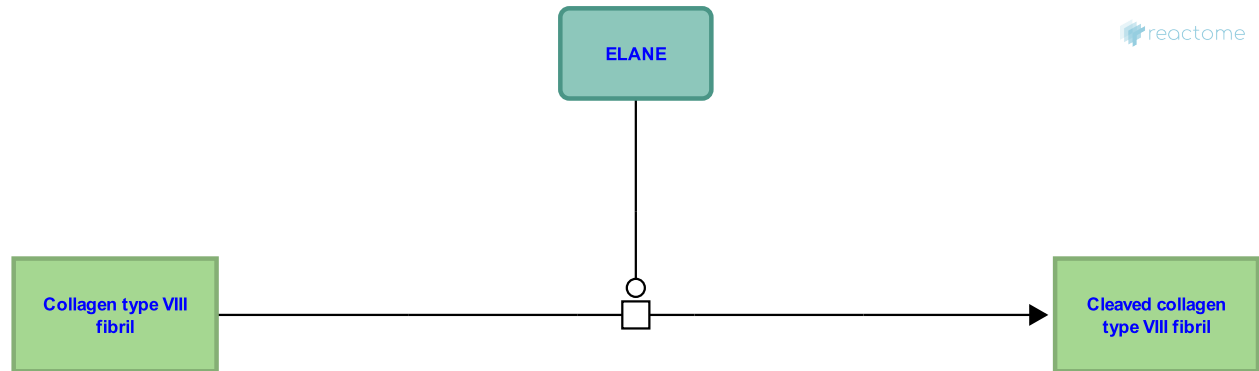
Location: [Collagen degradation](#)

Stable identifier: R-HSA-2482180

Type: transition

Compartments: extracellular region

Inferred from: [Cleavage of collagen type VIII by ELANE \(Homo sapiens\)](#)



Collagen type VIII is a short chain, network-forming collagen, thought to play a role in tissue remodeling and repair (Shuttleworth 1997, Weitkamp et al. 1999). There are two alpha chain subtypes, found in a ratio of two alpha-1 to one alpha-2 chains (Mann et al. 1990) in the typical collagen heterotrimer. Studies suggest that type VIII collagen is a major component of the hexagonal lattice seen in Descemet's membrane (Mann et al. 1990). Mutations in both alpha chains have been associated with Fuchs endothelial corneal dystrophy (FECD), a degenerative disease of the corneal endothelium (Jun et al. 2012).

Collagen type VIII can be degraded by neutrophil elastase (ELANE, ELA2; Kittelberger et al. 1992).

Followed by: [Gelatin degradation by MMP19](#), [Gelatin degradation by MMP1, 2, 3, 7, 8, 9, 12, 13](#)

Editions

2011-07-12	Authored	Jupe, S.
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Collagen type IX degradation by MMP3,13 ↗

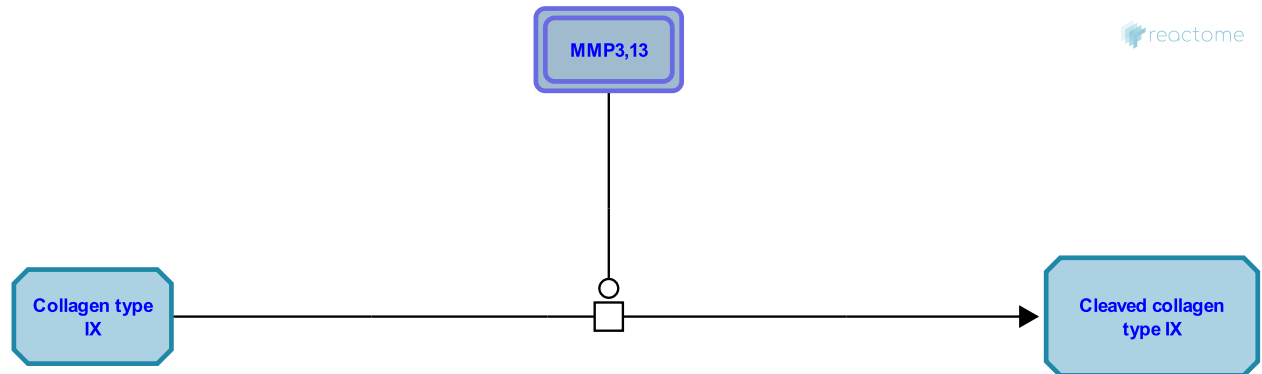
Location: [Collagen degradation](#)

Stable identifier: R-HSA-1564184

Type: transition

Compartments: extracellular region

Inferred from: [Collagen type IX degradation \(Bos taurus\)](#)



Type IX collagen interacts covalently with type II collagen fibril surfaces, suggesting that it represents a macromolecular bridge between fibrils and other cartilage matrix components (Eyre et al. 1987, Olsen 1997). Degradation of type IX (and type II) collagen is seen at the onset of inflammatory arthritis (Kojima et al. 2001).

Collagen type IX is cleaved by MMP3 (Okada et al. 1989, Eyre et al. 1991, Wu et al. 1991) and MMP13 (Knauper et al. 1997).

Followed by: [Gelatin degradation by MMP19](#), [Gelatin degradation by MMP1, 2, 3, 7, 8, 9, 12, 13](#)

Editions

2011-07-12	Authored	Jupe, S.
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Collagen type X degradation by MMP1,2 ↗

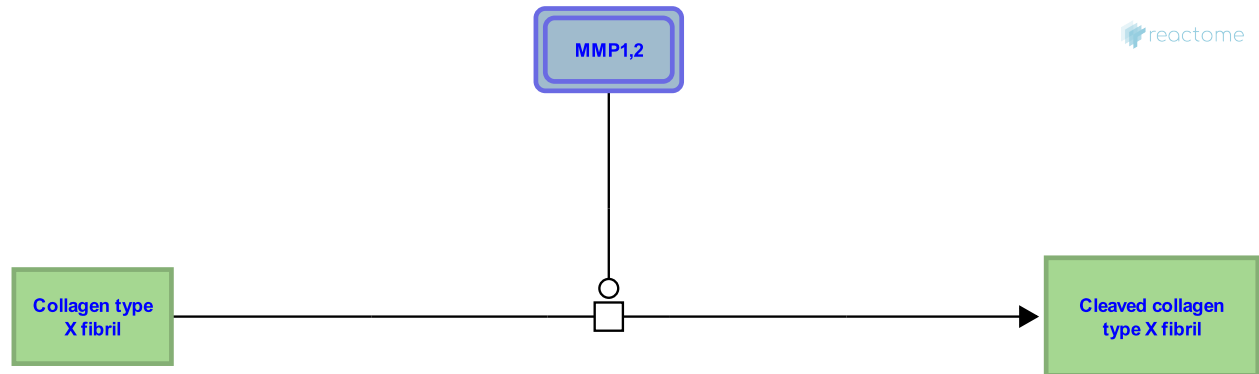
Location: [Collagen degradation](#)

Stable identifier: R-HSA-1564143

Type: transition

Compartments: extracellular region

Inferred from: [Collagen type X degradation by MMP1,2 \(Gallus gallus\)](#)



Collagen X is thought to form extended hexagonal networks (Kwan et al. 1991, Jacenko et al. 2001). It's distribution is limited to regions of hypertrophic cartilage destined for degradation during endochondral ossification (Schmid & Conrad 1982). It is also found in areas of surface fibrillation and osteophyte formation during the development of osteoarthritic lesions in articular cartilage (von der Mark et al. 1992). In Timp3 knockout mice type X collagen was observed mostly in areas of articular cartilage that stained strongly for collagen cleavage products, suggesting that deposition of type X collagen might be a damage repair mechanism (Sahebjam et al. 2007). Mutations in the gene COL10A1 are associated with Schmid/Japanese type metaphyseal chondrodysplasia (SMCD) (Warman et al. 1993, Ho et al. 2007, Woelfle et al. 2011).

Type X collagen is degraded by MMP1 (Schmid et al. 1986, Welgus et al. 1990, Cole et al. 1993), MMP2 (Cole et al. 1993, Welgus et al. 1990), MMP3 (Wu et al. 1991), MMP13 (Knauper et al. 1997) and neutrophil elastase (Kittelberger et al. 1992).

Followed by: [Gelatin degradation by MMP19](#), [Gelatin degradation by MMP1, 2, 3, 7, 8, 9, 12, 13](#)

Editions

2011-07-12	Authored	Jupe, S.
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Collagen type X degradation by MMP3, 13 ↗

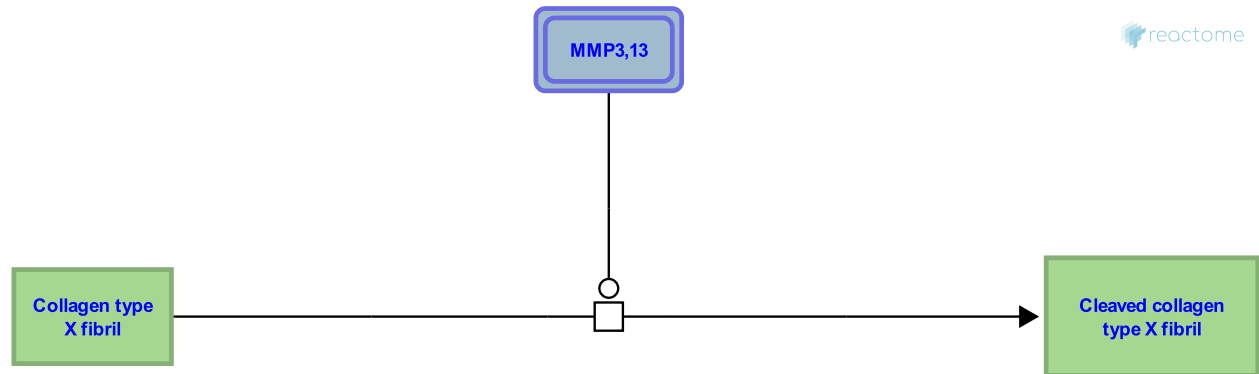
Location: [Collagen degradation](#)

Stable identifier: R-HSA-2484882

Type: transition

Compartments: extracellular region

Inferred from: [Collagen type X degradation by MMP3, 13 \(Homo sapiens\)](#)



Collagen X forms extended hexagonal networks (Kwan et al. 1991, Jacenko et al. 2001). It's distribution is limited to regions of hypertrophic cartilage destined for degradation during endochondral ossification (Schmid & Conrad 1982). It is also found in areas of surface fibrillation and osteophyte formation during the development of osteoarthritic lesions in articular cartilage (von der Mark et al. 1992). In Timp3 knockout mice type X collagen was observed mostly in areas of articular cartilage that stained strongly for collagen cleavage products, suggesting that deposition of type X collagen might be a damage repair mechanism (Sahebjam et al. 2007). Mutations in the gene COL10A1 are associated with Schmid/Japanese type metaphyseal chondrodysplasia (SMCD) (Warman et al. 1993, Ho et al. 2007, Woelfle et al. 2011).

Type X collagen is degraded by MMP1 (Schmid et al. 1986, Welgus et al. 1990, Cole et al. 1993), MMP2 (Cole et al. 1993, Welgus et al. 1990), MMP3 (Wu et al. 1991), MMP13 (Knauper et al. 1997) and ELANE (neutrophil elastase - Kittelberger et al. 1992).

Followed by: [Gelatin degradation by MMP19](#), [Gelatin degradation by MMP1, 2, 3, 7, 8, 9, 12, 13](#)

Editions

2011-07-12	Authored	Jupe, S.
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Collagen type XI degradation by MMP1,2,3,9 ↗

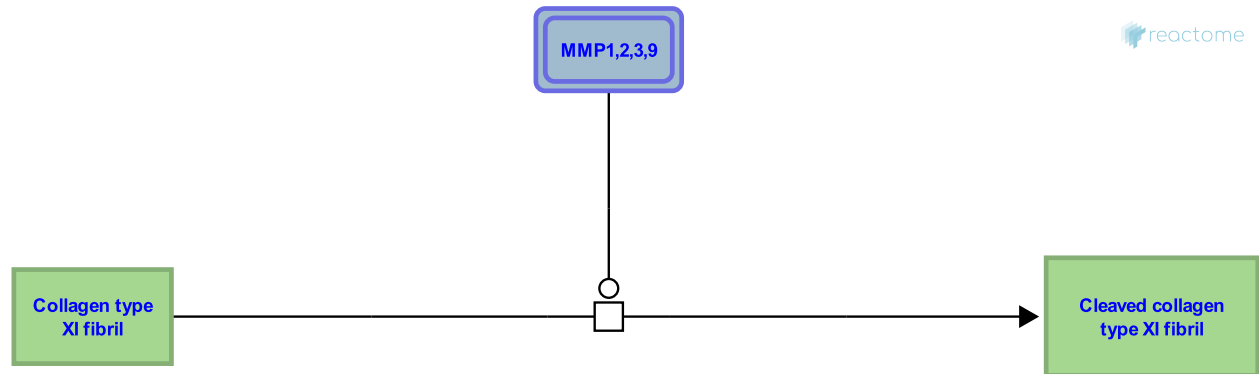
Location: [Collagen degradation](#)

Stable identifier: R-HSA-1564179

Type: transition

Compartments: extracellular region

Inferred from: [Collagen type XI degradation by MMP1,2,3,9 \(Bos taurus\)](#)



Collagen type XI has 3 types of alpha chain. The alpha1(XI) and alpha2(XI) chains are distinct gene products unique to collagen XI, while alpha3(XI) is a hyperglycosylated form of the alpha1 chain for collagen II (Burgeson & Hollister 1979, Morris & Bächinger 1987). Collagen type XI is a fibril-forming collagen found in conjunction with collagens type II and IX in cartilage fibrils (Miller & Gay 1987, Mendler et al. 1989). It is thought to be the structural equivalent of collagen V in connective tissue collagen fibrils. The formation of cartilage collagen fibrils requires collagen XI, suggesting a regulatory function (Li et al. 1995, Wu & Eyre 1995).

Mutations in COL11A1 result in fibrochondrogenesis, a severe, autosomal-recessive, short-limbed skeletal dysplasia (Tompson et al. 2010). Variations in COL11A1, COL11A2 and COL2A1 are associated with the inherited chondrodysplasias Marshall and Stickler syndromes (Annunen et al. 1999).

Collagen type XI is degraded by MMP1 (Eyre et al. 1984), MMP2 (Yu et al. 1990, Smith et al. 1991, Brown et al. 1996), MMP3 (Wu et al. 1991) and MMP9 (Hirose et al. 1992, Pormotabbed et al. 1994).

Followed by: [Gelatin degradation by MMP19](#), [Gelatin degradation by MMP1, 2, 3, 7, 8, 9, 12, 13](#)

Editions

2011-07-12	Authored	Jupe, S.
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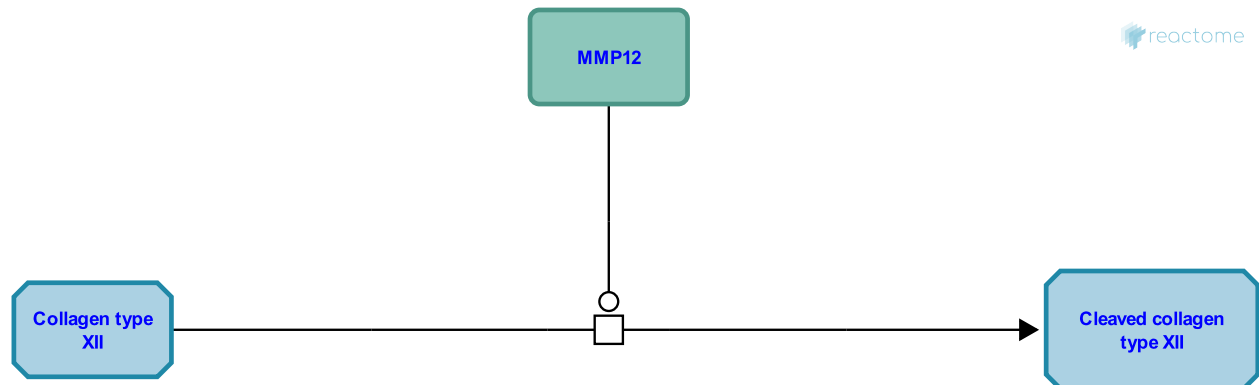
Collagen type XII degradation by MMP12 [↗](#)

Location: [Collagen degradation](#)

Stable identifier: R-HSA-2168046

Type: transition

Compartments: extracellular region



Collagen type XII is a member of the fibril-associated collagens with interrupted triple helices (FACIT) group, thought to be bound to the surface of interstitial collagen fibrils (Keene et al. 1991). It has only one alpha chain type, with two collagenous (Col1 and Col2) and three noncollagenous domains (NC1-NC3). Whereas the collagenous and the NC1 and NC2 regions are short, the NHE-terminal NC3 is a huge trimeric domain (Yamagata et al. 1991, Wälchli et al. 1993). Collagen XII may enhance the stability of connective tissues by bridging collagen fibrils (Nishiyama et al. 1994, Bader et al. 2009). It may be a stress response molecule, directly influenced by stretch and shear stress. Expression of COL12A1 is directly stimulated by mechanical forces (Flück et al. 2003, Jin et al. 2003, Arai et al. 2008). Expression is predominantly in bone, suggesting involvement of type XII collagen in the regulation of osteoblasts and cell interactions. Transgenic type XII collagen-null mice have skeletal abnormalities. They have decreased bone matrix deposition and delayed maturation. Compared with controls, Col12a knockout osteoblasts are disorganized, being less polarized with disrupted cell-cell interactions, decreased connexin43 expression and impaired gap junction function (Izu et al. 2011).

MMP12 can cleave collagen XII (Didangelos et al. 2011).

Followed by: [Gelatin degradation by MMP19](#), [Gelatin degradation by MMP1, 2, 3, 7, 8, 9, 12, 13](#)

Literature references

Didangelos, A., Yin, X., Mandal, K., Saje, A., Smith, A., Xu, Q. et al. (2011). Extracellular matrix composition and remodeling in human abdominal aortic aneurysms: a proteomics approach. *Mol Cell Proteomics*, 10, M111.008128. [↗](#)

Editions

2011-07-12	Authored	Jupe, S.
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Collagen type XIV degradation by MMP9,13 ↗

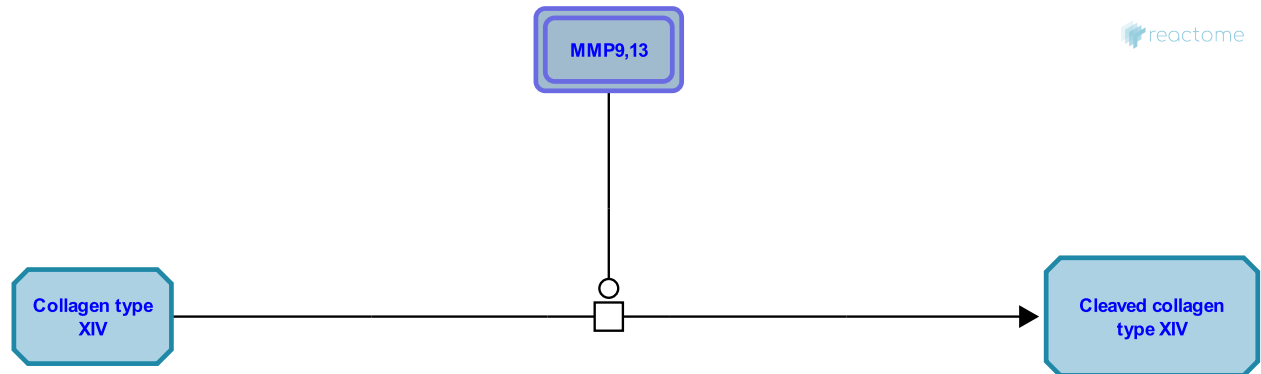
Location: [Collagen degradation](#)

Stable identifier: R-HSA-1564117

Type: transition

Compartments: extracellular region

Inferred from: [Collagen XIV degradation \(Bos taurus\)](#)



Collagen type XIV is a member of the fibril-associated collagens with interrupted triple helices (FACIT) family, expressed in most mesenchymal tissues. The non-collagenous domain at the N-terminus of collagen XIV is extremely large, nearly 80% of the entire polypeptide. This domain is composed of eight fibronectin type III repeats, two von Willebrand factor A-like (vWFA) domains and one non-collagenous domain 4 (NC4 domain) related to collagen type IX. Collagen XIV is expressed in most mesenchymal tissues where it appears to interact with collagen type VI, glycosaminoglycans, proteoglycans and matrix receptors (Brown et al. 1993, Imhof & Trueb 1998). It has been implicated as a regulator of fibrillogenesis. Collagen type XIV deficient mice have a grossly normal phenotype but their skin has altered mechanical properties. Tendons were seen to be enlarged at postnatal day 4 though mature tendons appeared normal. Tendons from postnatal day 7 KO mice had reduced strength but by 60 days were comparable with wild-type (Ansorge et al. 2009). Adult Col14a1 mice have defects in ventricular morphogenesis (Tao et al. 2012).

Collagen type XIV is degraded by MMP9 (Sires et al. 1995) and MMP13 (Knauper et al. 1997).

Followed by: [Gelatin degradation by MMP19](#), [Gelatin degradation by MMP1, 2, 3, 7, 8, 9, 12, 13](#)

Editions

2011-07-12	Authored	Jupe, S.
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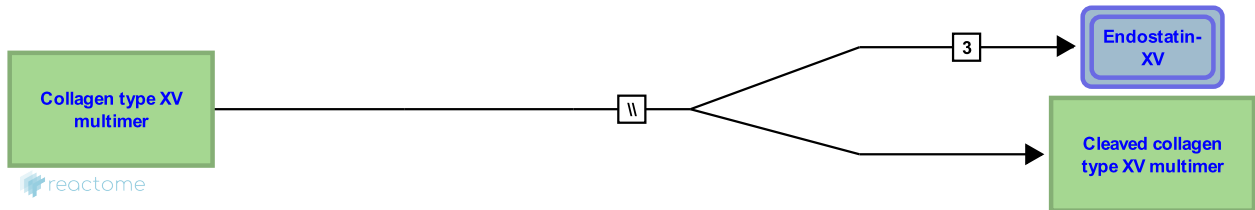
Collagen type XV restin release ↗

Location: [Collagen degradation](#)

Stable identifier: R-HSA-2168038

Type: omitted

Compartments: extracellular region



Collagens type XV and XVIII are closely related non-fibrillar collagens that define the multiplexin (multiple triple helix domains with interruptions) subfamily of collagens. Both are homotrimers characterized by highly interrupted collagenous domains flanked by large globular domains with attached glycosaminoglycan chains. Collagen XV is localized in the outermost layer of the basement membrane (BM) and in the fibrillar matrix. Collagen type XV is the only collagen able to self-assemble into higher-order cruciform structures with intermolecular binding sites (Myers et al. 2007). The interaction is mediated by interactions between triple helical regions (Hurskainen et al. 2010). It is predominantly located in the basement membranes of microvessels, and cardiac and skeletal myocytes (Hägg et al. 1997), where it binds basement membrane and microfibrillar components such as fibulin-2, nidogen-2, vitronectin, laminin, and fibronectin (Sasaki et al. 2000, Hurskainen et al. 2010). It may form a bridge between fibrillar collagens and the basement membrane (Amenta et al. 2005), acting as a molecular shock absorber to stabilize and enhance resilience to compressive and expansive forces (Myers et al. 2007). Lack of Collagen type XV in Col15a1-null mice resulted in increased permeability and impaired microvascular hemodynamics, distinct early-onset and age-dependent defects in heart structure and function, a poorly organized fibrillar collagen matrix with marked interstitial deposition of nonfibrillar protein aggregates, increased tissue stiffness, and irregularly organized cardiomyocytes (Rasi et al. 2010a). Col15a1 knockout also leads to loosely packed axons in C-fibers and polyaxonal myelination. Simultaneous knockout with laminin alpha-4 leads to severely impaired radial sorting and myelination (Rasi et al. 2010b).

The C-terminal non-collagenous region of collagen type XV is known as restin because it resembles endostatin, having antiangiogenic effects (Ramchandran et al. 1999, Sasaki et al. 2000).

Literature references

Ramchandran, R., Dhanabal, M., Volk, R., Waterman, MJ., Segal, M., Lu, H. et al. (1999). Antiangiogenic activity of restin, NC10 domain of human collagen XV: comparison to endostatin. *Biochem Biophys Res Commun*, 255, 735-9.

↗

Editions

2011-07-12	Authored	Jupe, S.
2012-10-08	Reviewed	Sorsa, T.
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Collagen type XVI degradation by MMP9 ↗

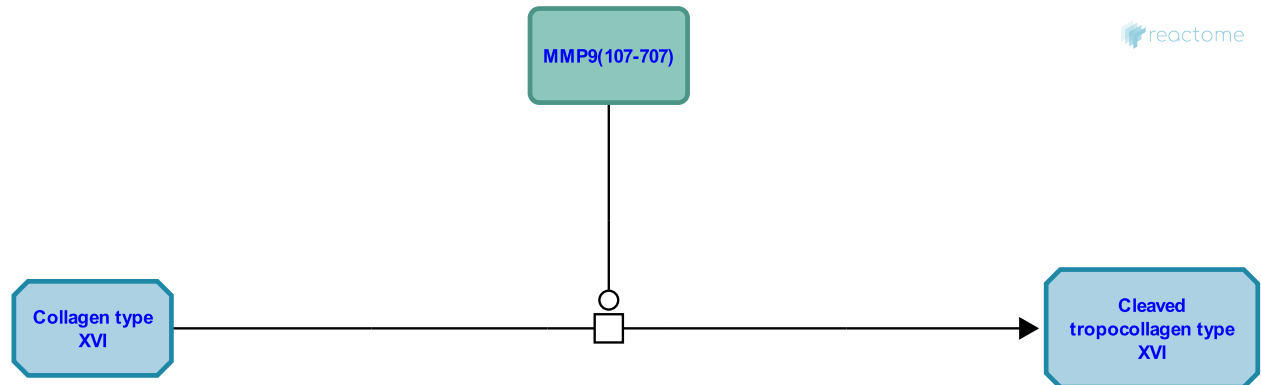
Location: [Collagen degradation](#)

Stable identifier: R-HSA-2168982

Type: transition

Compartments: extracellular region

Inferred from: [Collagen type XVI degradation \(Bos taurus\)](#)



Type XVI collagen is a member of the FACIT collagen family (fibril-associated collagens with interrupted helices). During early mouse development, it occurs in many tissues and is co-distributed with the major fibrillar collagens (Lai & Chu 1996). In skin, collagen XVI preferentially occurs in narrow zones near basement membranes at the dermo-epidermal junction (DEJ) of blood vessels (Grässel et al., 1999). In papillary dermis, the protein unexpectedly does not occur in banded collagen fibrils, but is a component of specialized fibrillin-1-containing microfibrils. However, in cartilage matrix it does not aggregate with fibrillin-1, rather it exists as a discrete population of thin, weakly banded collagen fibrils in association with collagens II and XI (Kassner et al. 2003, 2004). Collagen XVI induces the recruitment of integrins alpha1 beta1 and alpha1 beta 2 into focal adhesion plaques, a principal step in integrin signaling (Eble et al. 2006), allowing cells to affect the architecture of the ECM networks by binding and moving ECM proteins.

Collagen type XVI is cleaved by MMP9 (Sires et al. 1995).

Followed by: [Gelatin degradation by MMP19](#), [Gelatin degradation by MMP1, 2, 3, 7, 8, 9, 12, 13](#)

Editions

2011-07-12	Authored	Jupe, S.
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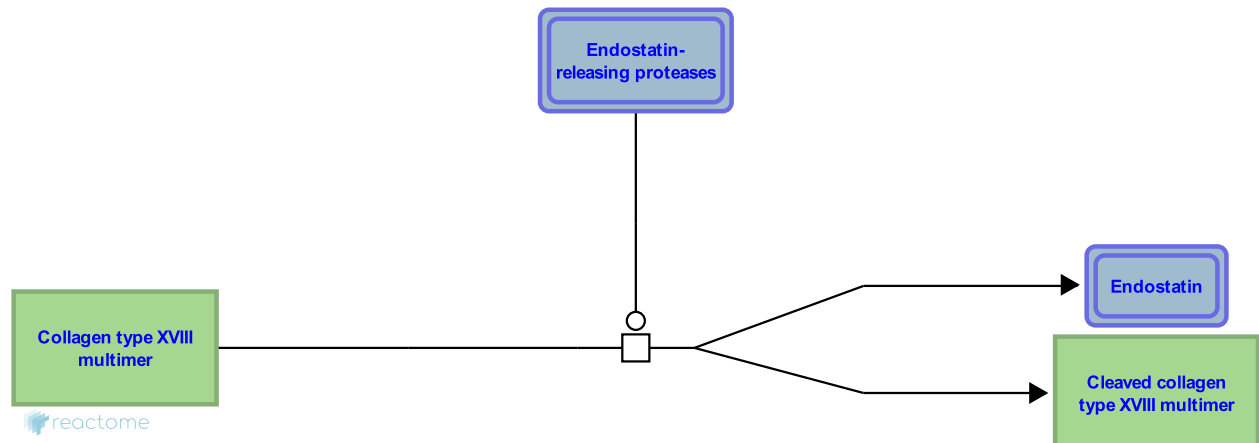
Collagen type XVIII endostatin release [↗](#)

Location: [Collagen degradation](#)

Stable identifier: R-HSA-2168923

Type: transition

Compartments: extracellular region



Collagen type XVIII is a heparan sulfate proteoglycan associated with the basement membranes of almost all epithelia and endothelia. It has a large C-terminal noncollagenous domain. Mouse knockouts suggest that it may have a role in maintaining the structural integrity of the extracellular matrix (Utriainen et al. 2004).

Proteolytic cleavage of the C-terminal noncollagenous domain by matrix metalloproteinases (Heljasvaara et al. 2005) releases 18 to 38 kDa C-terminal proteolytic fragments, collectively named endostatin. They have anti-angiogenic activity (O'Reilly et al. 1997, Ständker et al. 1997) and suppress primary tumor and metastasis growth in experimental animal models (Ortega & Werb 2002). It is not clear whether this collagen subtype forms supramolecular assemblies (Myllyharju & Kivirikko, 2004) but thought likely, via a similar mechanism to the related collagen XV (Hurskainen et al. 2010).

Endostatin-like fragments are released from collagen type XVIII by MMP 7 (Lin et al. 2001), 3, 9, 12, 13 (Ferrerias et al. 2000) and 20 (Heljasvaara et al. 2005). Several cathepsins and elastase can bring about endostatin release (Ferrerias et al. 2000, Felbor et al. 2000).

Literature references

Ferrerias, M., Felbor, U., Lenhard, T., Olsen, BR., Delaissé, J. (2000). Generation and degradation of human endostatin proteins by various proteinases. *FEBS Lett.*, 486, 247-51. [↗](#)

Heljasvaara, R., Nyberg, P., Luostarinen, J., Parikka, M., Heikkilä, P., Rehn, M. et al. (2005). Generation of biologically active endostatin fragments from human collagen XVIII by distinct matrix metalloproteinases. *Exp Cell Res*, 307, 292-304. [↗](#)

Editions

2011-07-12	Authored	Jupe, S.
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Endostatin degradation by cathepsins [↗](#)

Location: [Collagen degradation](#)

Stable identifier: R-HSA-2471621

Type: omitted

Compartments: extracellular region



As well as generating endostatin from collagen XVIII, cathepsins L and B quickly degrade it, as do cathepsins D and K. In contrast MMPs that produce endostatin do not cleave it further (Ferrerias et al. 2000).

Literature references

Ferrerias, M., Felbor, U., Lenhard, T., Olsen, BR., Delaissé, J. (2000). Generation and degradation of human endostatin proteins by various proteinases. *FEBS Lett.*, 486, 247-51. [↗](#)

Editions

2011-07-12	Authored	Jupe, S.
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Collagen type XIX degradation [↗](#)

Location: [Collagen degradation](#)

Stable identifier: R-HSA-2172433

Type: omitted

Compartments: extracellular region



Collagen type XIX is a FACIT (fibril-associated collagens with interrupted triple helix) collagen family member (Inoguchi et al. 1995) with a large non-collagenous N terminal domain that can self-assemble into higher order structures that are stabilized by intermolecular disulfide cross-links. Collagen type XIX is the least abundant collagen so far purified, comprising ~10-6% of dry weight in human umbilical cord (Myers et al. 2003). It is found in the basement membrane (BM) of normal human tissues. In developing embryos it is transiently expressed in certain muscular tissues and brain areas. Due to this localized expression, it is thought to be involved in the formation of specialized BM zones (Sumiyoshi et al. 2001). Collagen XIX is lost early in the development of invasive tumours, prior to penetration and eventual dissolution of the epithelial BM (Amenta et al. 2003). The NC1 domain of type XIX collagen exerts antitumor activity (Ramont et al. 2007).

Literature references

Amenta, PS., Hadad, S., Lee, MT., Barnard, N., Li, D., Myers, JC. (2003). Loss of types XV and XIX collagen precedes basement membrane invasion in ductal carcinoma of the female breast. *J Pathol*, 199, 298-308. [↗](#)

Editions

2011-07-12	Authored	Jupe, S.
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2012-11-12	Edited	Jupe, S.

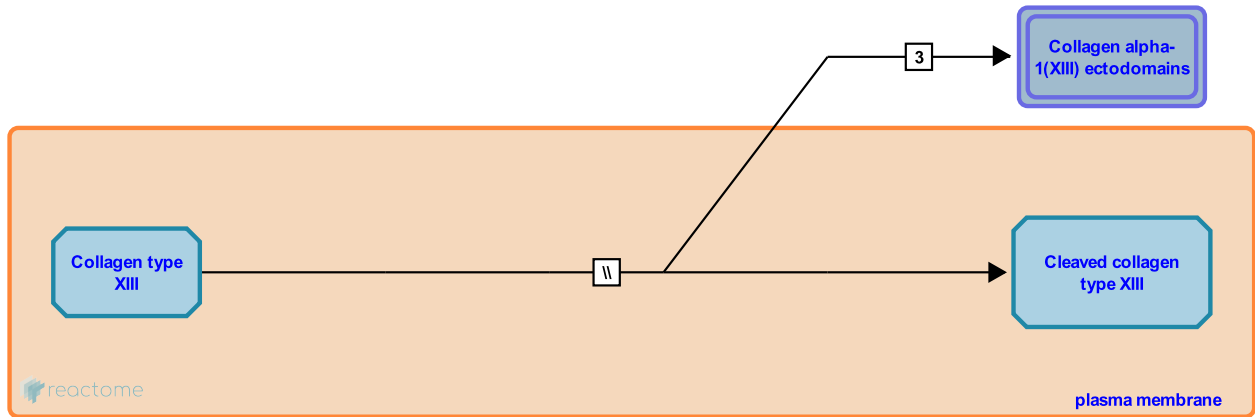
Collagen type XIII ectodomain shedding [↗](#)

Location: [Collagen degradation](#)

Stable identifier: R-HSA-2167942

Type: omitted

Compartments: plasma membrane



Type XIII is a non-fibril-forming type II transmembrane protein with a large amino terminal NC1 domain. This domain has a hydrophobic membrane-spanning segment that anchors the molecule to the plasma membrane and a large extracellular, mostly collagenous carboxyterminal domain (Hägg et al. 1998). Recombinant type XIII collagen can form homotrimers with triple-helical collagenous domains (Snellman et al. 2000a). It is detected at low levels in all connective tissue-producing cells; in cultured cells it is localized in focal adhesions (Hägg et al. 2001). The extracellular region has an adhesion-related function (Hägg et al. 2001) that is involved in formation of the neuromuscular junction (Latvanlehto et al. 2010). The purified protein has been shown to interact with Integrin alpha1beta1 (Nykvist et al. 2000). An N-terminal ectodomain portion of type XIII collagen is cleaved in culture medium by a furin-like protease (Snellman et al. 2000b, Väisänen et al. 2004). This ectodomain interacts with fibronectin, nidogen-2 and perlecan (Tu et al. 2002, Väisänen et al. 2006).

Literature references

Snellman, A., Tu, H., Väisänen, T., Kvist, AP., Huhtala, P., Pihlajaniemi, T. (2000). A short sequence in the N-terminal region is required for the trimerization of type XIII collagen and is conserved in other collagenous transmembrane proteins. *EMBO J.*, 19, 5051-9. [↗](#)

Väisänen, MR., Väisänen, T., Pihlajaniemi, T. (2004). The shed ectodomain of type XIII collagen affects cell behaviour in a matrix-dependent manner. *Biochem. J.*, 380, 685-93. [↗](#)

Editions

2011-07-12	Authored	Jupe, S.
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Collagen type XVII ectodomain shedding [↗](#)

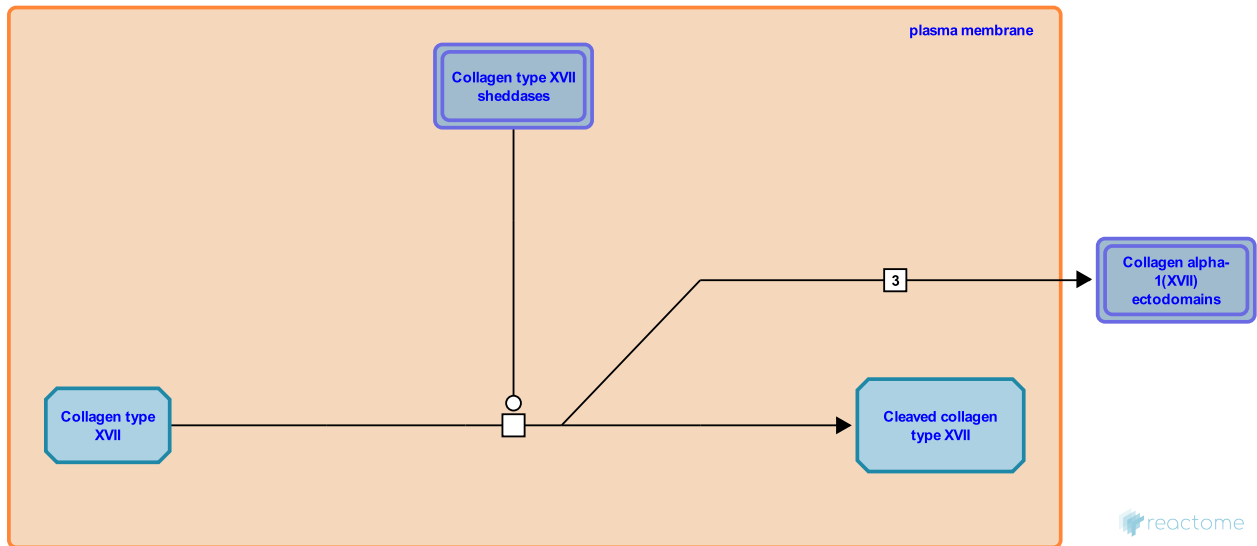
Location: [Collagen degradation](#)

Stable identifier: R-HSA-2168960

Type: transition

Compartments: plasma membrane

Inferred from: [Collagen type XVII ectodomain shedding \(Homo sapiens\)](#)



Collagen type XVII, identified as the 180-kDa bullous pemphigoid antigen or BP180, is a transmembrane protein forming a family with collagen type XIII. It is an important structural component of hemidesmosomes, complexes found in the dermal-epidermal basement membrane zone that mediate adhesion of keratinocytes to the underlying membrane (Franzke et al. 2005). The intracellular ligands of collagen XVII include Beta 4-integrins, plectin and BP230 in the hemidesmosomal plaque (Koster et al. 2003). Extracellular ligands include alpha 6-integrin and laminin-5 in anchoring filaments (Hopkinson et al. 1995, Tasanen et al. 2004). Mutations in the human collagen XVII gene COL17A1 lead to diminished epidermal adhesion and skin blistering in response to minimal shearing forces, a disorder called junctional epidermolysis bullosa (JEB).

A soluble ectodomain form of collagen type XVII referred to as LAD-1 is generated by proteolytic processing of the full length form (Hirako et al. 1988, Schäcke et al. 1998). Collagen XVII has a furin consensus sequence but is cleaved by proteinases of the ADAM family rather than furin convertases. ADAM-17 (TACE) appears to be the major physiologically-relevant sheddase for collagen XVII, though ADAM-9 and -10 may substitute (Franzke et al. 2002). These proteinases are activated by furin (Franzke et al. 2005).

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Collagen type XXIII ectodomain shedding [↗](#)

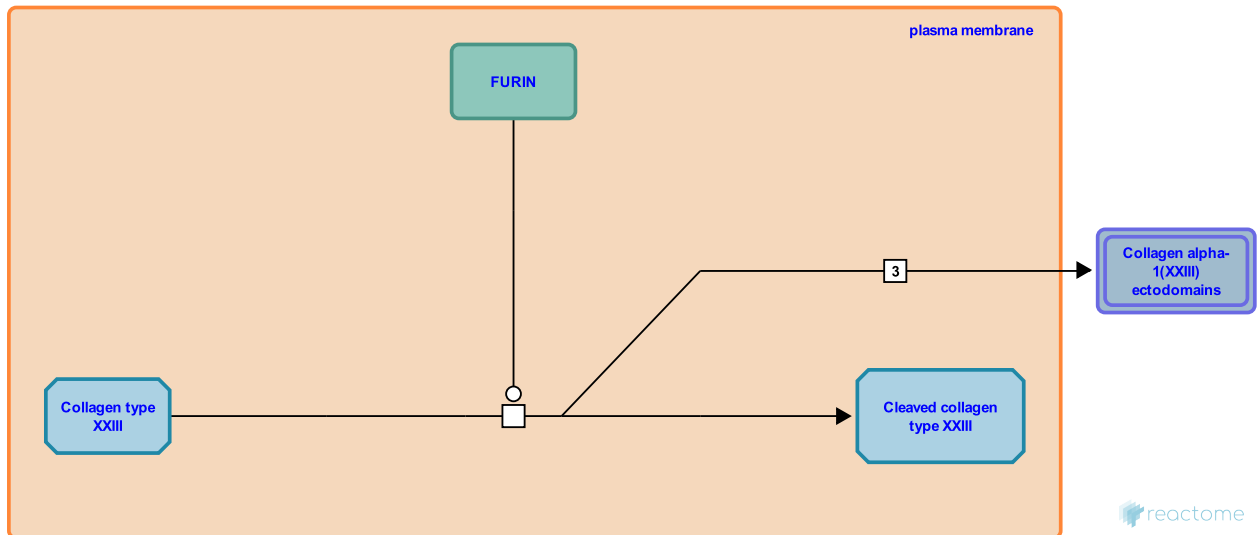
Location: [Collagen degradation](#)

Stable identifier: R-HSA-2172405

Type: transition

Compartments: plasma membrane

Inferred from: [Collagen type XXIII ectodomain shedding \(Mus musculus\)](#)



Collagen type XXIII is a type II transmembrane collagen with a relatively small ectodomain. It exists in a membrane-bound form and a shed form, cleaved by furin (Veit et al. 2007). Both forms can bind $\alpha 2\beta 1$ integrin via the ectodomain, stimulating the formation of focal adhesion plaques (Veit et al. 2011).

Editions

2011-07-12	Authored	Jupe, S.
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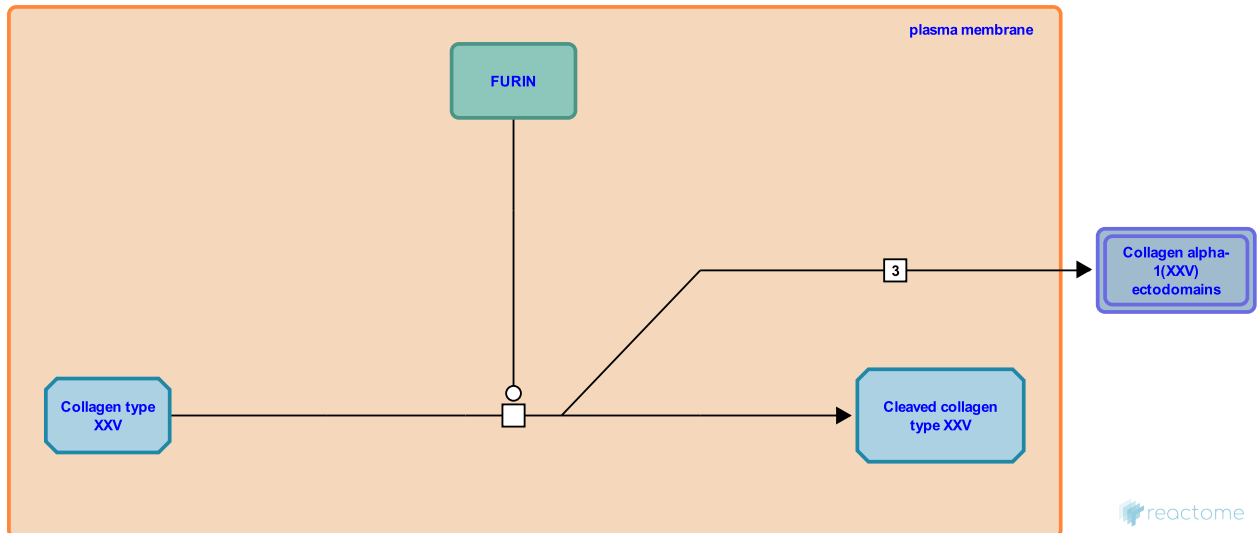
Collagen type XXV ectomain shedding [↗](#)

Location: [Collagen degradation](#)

Stable identifier: R-HSA-2471842

Type: transition

Compartments: plasma membrane



Identified as a component of amyloid plaques in Alzheimer's brain, the ectodomain of type XXV collagen (known as CLAC) is released by furin convertase activity (Hashimoto et al. 2002). The presence of CLAC leads to Abeta fibril bundles that have an increased resistance to proteases (Söderberg et al. 2005).

Literature references

Hashimoto, T., Wakabayashi, T., Watanabe, A., Kowa, H., Hosoda, R., Nakamura, A. et al. (2002). CLAC: a novel Alzheimer amyloid plaque component derived from a transmembrane precursor, CLAC-P/collagen type XXV. *EMBO J.*, 21, 1524-34. [↗](#)

Editions

2011-07-12	Authored	Jupe, S.
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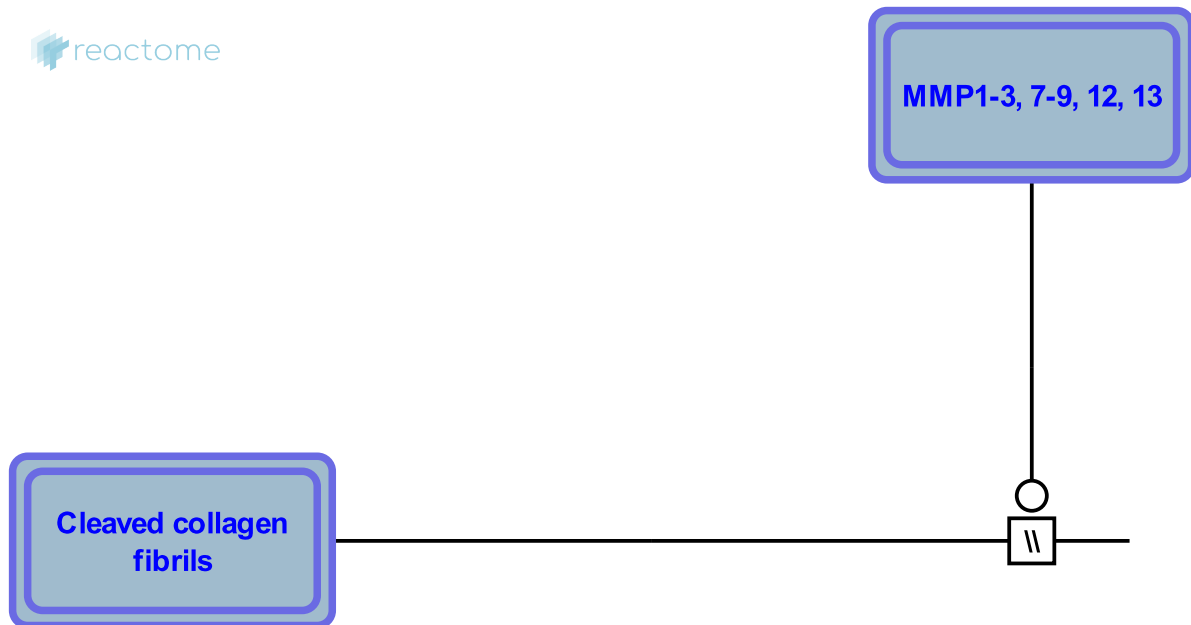
Gelatin degradation by MMP1, 2, 3, 7, 8, 9, 12, 13 ↗

Location: [Collagen degradation](#)

Stable identifier: R-HSA-1454757

Type: omitted

Compartments: extracellular region



Gelatin is formed when collagen becomes partly or completely uncoiled when compared with the regular triple helix structure of fibrillar collagen. In vivo, once collagens are initially cleaved into classical 3/4 and 1/4 fragments (by collagenases) they rapidly denature at body temperature and are degraded by gelatinases and other nonspecific tissue proteinases (Chung et al. 2004) to a semi-solid colloid gel. MMP2 and MMP9 are the major gelatinases (Collier et al. 1988, Wilhelm et al. 1989) often referred to respectively as Gelatinase A and Gelatinase B (Murphy & Crabbe 1995). However many other MMPs have gelatinase activity, including MMP1 (Murphy et al. 1982, Isaksen & Fagerhol 2001, Chung et al. 2004), MMP3 (Chin et al. 1985, Isaksen & Fagerhol 2001), MMP7 (Isaksen & Fagerhol 2001), MMP8 (Isaksen & Fagerhol 2001), MMP10 (Sanches-Lopez et al. 1993), MMP12 (Chandler et al. 1996), MMP13 (Knäuper et al. 1993, Isaksen & Fagerhol 2001), MMP16 (Shofuda et al. 1997), MMP17 (Wang et al. 1999), MMP18 (Spinucci et al. 1988), MMP19 (Stracke et al. 2000) and MMP22 (Yang & Kurkinen 1998).

Preceded by: [Collagen type I degradation by MMP1,2,8,13, PRSS2](#), [Collagen type I degradation by MMP14](#), [Collagen type I degradation by MMP15](#), [Collagen type II degradation by MMP1,3,8,13,PRSS2](#), [Collagen type II degradation by MMP14](#), [Collagen type III degradation by MMP1,8,9,13](#), [Collagen type III degradation by MMP10](#), [Collagen type III degradation by MMP14](#), [Collagen type IV degradation by MMP2,3,4,9,10,12](#), [Collagen type V degradation by MMP2,9,10](#), [Collagen type VI degradation by MMP2,9,11](#), [Collagen type VII degradation by MMP1,2,3](#), [Collagen type VIII degradation by ELANE](#), [Collagen type VIII degradation by MMP1](#), [Collagen type IX degradation by MMP3,13](#), [Collagen type X degradation by MMP1,2](#), [Collagen type X degradation by MMP3, 13](#), [Collagen type XI degradation by MMP1,2,3,9](#), [Collagen type XII degradation by MMP12](#), [Collagen type XIV degradation by MMP9,13](#), [Collagen type XVI degradation by MMP9](#)

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Editions

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Gelatin degradation by MMP19 ↗

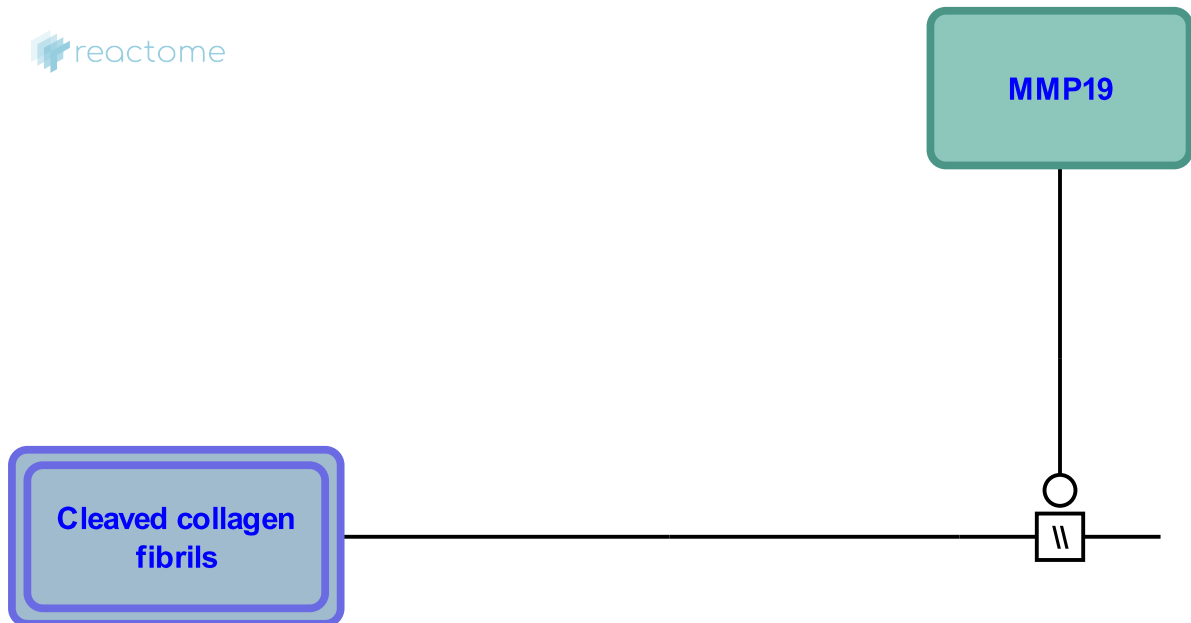
Location: [Collagen degradation](#)

Stable identifier: R-HSA-2537499

Type: omitted

Compartments: extracellular region

Inferred from: [Gelatin degradation by MMP19 \(Homo sapiens\)](#)



Gelatin is formed when collagen becomes partly or completely uncoiled when compared with the regular triple helix structure of fibrillar collagen. In vivo, once collagens are initially cleaved into classical 3/4 and 1/4 fragments (by collagenases) they rapidly denature at body temperature and are degraded by gelatinases and other nonspecific tissue proteinases (Chung et al. 2004) to a semi-solid colloid gel. MMP2 and MMP9 are the major gelatinases (Collier et al. 1988, Wilhelm et al. 1989) often referred to respectively as Gelatinase A and Gelatinase B (Murphy & Crabbe 1995). However many other MMPs have gelatinase activity, including MMP1 (Murphy et al. 1982, Isaksen & Fagerhol 2001, Chung et al. 2004), MMP3 (Chin et al. 1985, Isaksen & Fagerhol 2001), MMP7 (Isaksen & Fagerhol 2001), MMP8 (Isaksen & Fagerhol 2001), MMP10 (Sanches-Lopez et al. 1993), MMP12 (Chandler et al. 1996), MMP13 (Knäuper et al. 1993, Isaksen & Fagerhol 2001), MMP16 (Shofuda et al. 1997), MMP17 (Wang et al. 1999), MMP18 (Spinucci et al. 1988), MMP19 (Stracke et al. 2000) and MMP22 (Yang & Kurkinen 1998).

Preceded by: [Collagen type I degradation by MMP1,2,8,13, PRSS2](#), [Collagen type I degradation by MMP14](#), [Collagen type I degradation by MMP15](#), [Collagen type II degradation by MMP1,3,8,13,PRSS2](#), [Collagen type II degradation by MMP14](#), [Collagen type III degradation by MMP1,8,9,13](#), [Collagen type III degradation by MMP10](#), [Collagen type III degradation by MMP14](#), [Collagen type IV degradation by MMP2,3,4,9,10,12](#), [Collagen type V degradation by MMP2,9,10](#), [Collagen type VI degradation by MMP2,9,11](#), [Collagen type VII degradation by MMP1,2,3](#), [Collagen type VIII degradation by ELANE](#), [Collagen type VIII degradation by MMP1](#), [Collagen type IX degradation by MMP3,13](#), [Collagen type X degradation by MMP1,2](#), [Collagen type X degradation by MMP3, 13](#), [Collagen type XI degradation by MMP1,2,3,9](#), [Collagen type XII degradation by MMP12](#), [Collagen type XIV degradation by MMP9,13](#), [Collagen type XVI degradation by MMP9](#)

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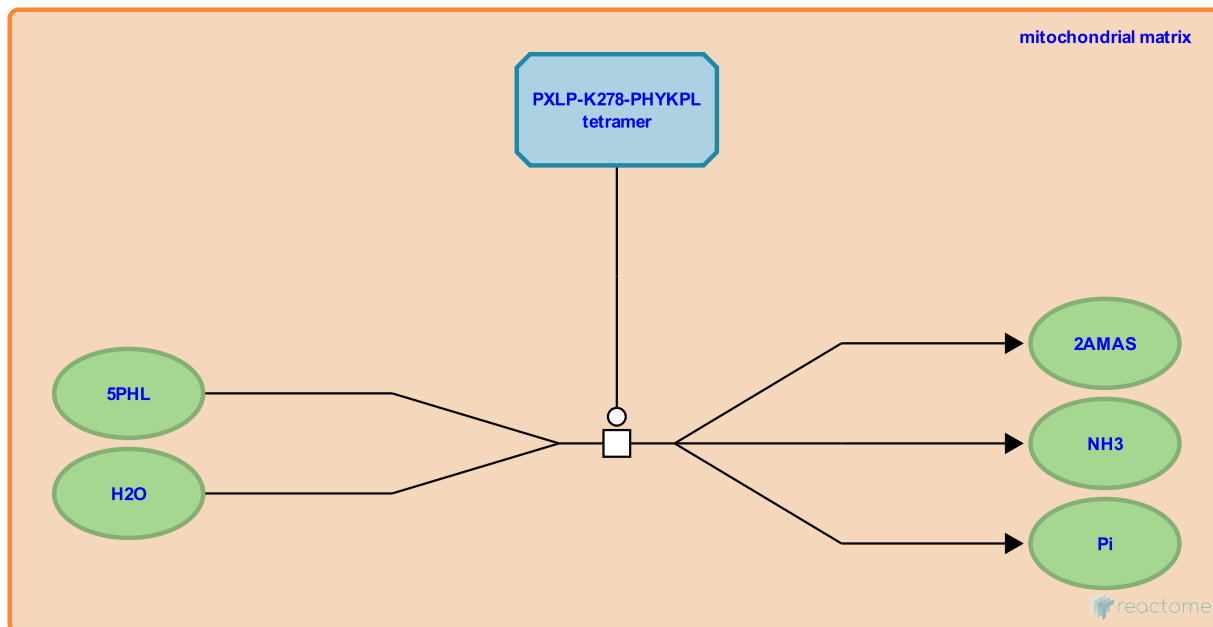
PXLP-K278-PHYKPL tetramer hydrolyses 5PHL [↗](#)

Location: [Collagen degradation](#)

Stable identifier: R-HSA-5696408

Type: transition

Compartments: mitochondrial matrix



In mitochondria, ethanolamine-phosphate phospho-lyase and 5-phosphohydroxy-L-lysine phospho-lyase (ETNPPL and PHYKPL respectively) are two closely related pyridoxal-phosphate-dependent, homotetrameric ammoniophospholyases that hydrolyse phosphoethanolamine (PETA) and 5-phosphohydroxylysine (5PHL) respectively (Veiga-da-Cunha et al. 2012). PETA is a component and a precursor of phospholipids whereas 5PHL is a breakdown product of collagen. ETNPPL utilises one pyridoxal 5'-phosphate (PXLP) as cofactor per subunit.

Literature references

Veiga-da-Cunha, M., Hadi, F., Balligand, T., Stroobant, V., Van Schaftingen, E. (2012). Molecular identification of hydroxylysine kinase and of ammoniophospholyases acting on 5-phosphohydroxy-L-lysine and phosphoethanolamine. *J. Biol. Chem.*, 287, 7246-55. [↗](#)

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2015-06-26	Reviewed	D'Eustachio, P.

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