Collagen degradation

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**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**


Reactome database release: 79

This document contains 1 pathway and 34 reactions (see Table of Contents)
Collagen fibril diameter and spatial organisation are dependent on the species, tissue type and stage of development (Parry 1988). The lengths of collagen fibrils in mature tissues are largely unknown but in tendon can be measured in millimetres (Craig et al. 1989). Collagen fibrils isolated from adult bovine corneal stroma had ~350 collagen molecules in transverse section, tapering down to three molecules at the growing tip (Holmes & Kadler 2005).

The classical view of collagenases is that they actively unwind the triple helical chain, a process termed molecular tectonics (Overall 2002, Bode & Maskos 2003), before preferentially cleaving the alpha2 chain followed by the remaining chains (Chung et al. 2004). More recently it has been suggested that collagen fibrils exist in an equilibrium between protected and vulnerable states (Stultz 2002, Nerenberg & Stultz 2008). The prototypical triple-helical structure of collagen does not fit into the active site of collagenase MMPs. In addition the scissile bonds are not solvent-exposed and are therefore inaccessible to the collagenase active site (Chung et al. 2004, Stultz 2002). It was realized that collagen must locally unfold into non-triple helical regions to allow collagenolysis. Observations using circular dichroism and differential scanning calorimetry confirm that there is considerable heterogeneity along collagen fibres (Makareeva et al. 2008) allowing access for MMPs at physiological temperatures (Salsas-Escat et al. 2010).

Collagen fibrils with cut chains are unstable and accessible to proteinases that cannot cleave intact collagen strands (Woessner & Nagase 2000, Somerville et al. 2003). Continued degradation leads to the formation of gelatin (Lovejoy et al. 1999). Degradation of collagen types other than I-III is less well characterized but believed to occur in a similar manner.

Metalloproteinases (MMPs) play a major part in the degradation of several extracellular macromolecules including collagens. MMP1 (Welgus et al. 1981), MMP8 (Hasty et al. 1987), and MMP13 (Knauper et al. 1996), sometimes referred to as collagenases I, II and III respectively, are able to initiate the intrahelical
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**


**Editions**

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

Location: Collagen degradation

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