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## Cell-associated MT1-MMP degrades collagen type I

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## Keywords

Collagen type I, MT1-MMP

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## Context

Membrane-type matrix metalloproteinases (MT-MMPs) are, unlike the other MMPs, attached to the cell surface. A recognized function of MT1-MMP is the activation of gelatinase A (MMP-2). However, MT1-MMP itself may also directly exert proteolytic activity. The severe defects observed in MT1-MMP knockout mice, mainly bony malformations, suggest an important role of MT1-MMP in collagen type I turnover. Previous experiments have investigated MT-MMP activity using recombinant, soluble MT-MMP. In the present paper, however, a cell culture model was used to investigate the collagenolytic capacity of MT1-MMP attached to the cell surface.

## Significant findings

The results of this study indicate that MT1-MMP is a potent cell associated interstitial collagenase. Cells over-expressing MT1-MMP degraded collagen type I up to four times more efficiently than the control cells. Tissue inhibitor of matrix metalloproteinases (TIMP)-2, but not TIMP-1 inhibited collagenolysis (TIMP-2, unlike TIMP-1, is an efficient inhibitor of MT1-MMP). Collagenolysis was inhibited by ionomycin, an inhibitor of MT1-MMP maturation.

## Comments

The findings of this study suggest an important role of MT1-MMP in pericellular collagen type I degradation. In diseases such rheumatoid arthritis, excessive collagen degradation occurs in the articular cartilage and bone, leading to irreversible joint damage. As a high level of expression of MT1-MMP has

been observed in the rheumatoid synovium, MT1-MMP may be an important mediator of cartilage and bone erosion. Before MT1-MMP can be considered as an interesting target for joint-sparing therapy, further studies need to be carried out investigating the role of MT1-MMP in cartilage and bone destruction, for instance by studying the proteolytic potential of MT1-MMP on collagen type II and other proteins of the articular cartilage and bone.

## Methods

Immunofluorescence, transfection, tet-off system, <sup>14</sup>C-labelled collagen films, gelatin zymography, Western blotting

## Additional information

## References

1. Atkinson SJ, Patterson ML, Butler MJ, Murphy G: Membrane type 1 matrix metalloproteinase and gelatinase A synergistically degrade type 1 collagen in a cell model. FEBS Lett. 2001, 491: 222-226.