Studies on the destruction of articular cartilage by matrix metalloproteinases

1996 Fiscal Year Final Research Report Summary

Studies on the destruction of articular cartilage by matrix metalloproteinases

Research Project

Project/Area Number

07457049

Research Category

Grant-in-Aid for Scientific Research (B)

Allocation Type

Single-year Grants

Section

一般

Research Field

Human pathology

Research Institution

Kanazawa University

Principal Investigator

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Project Period (FY)

1995 – 1996

Keywords

Matrix metalloproteinase / Rheumatoid arthritis / Osteoarthritis / Cartilage destruction / Degradation / Tissue inhibitor / Cytokine / Activation

Research Abstract

Matrix metalloproteinases (MMPs) are composed of at least 15 different molecules and their activities are strictly regulated by their common tissue inhibitors of metalloproteinases (TIMP-1,2,3,4). In the present studies, we have demonstrated that membrane-type 1 matrix metalloproteinase (MT1-MMP) is highly expressed in the human osteoarthritic cartilage showing a positive correlation with activation of proMMP-2 (progelatinase A).

We have also revealed that MT1-MMP is an extracellular matrix (ECM) -degrading proteinase capable of digesting interstitial collagens and aggrecan as well as an activator of proMMP-2. In osteoarthritis and rheumatoid arthritis, cartilage matrix protein and SPARC were overexpressed, suggesting that it may be a tissue reaction secondary to the degradation of the ECM components by MMPs expressed in the cartilages. Actually, TGF-beta which stimulates ECM production in various mesenchymal cells was released after degradation of the TGF-beta/decorin complex by MMPs. To determine the production levels, sandwich enzyme immunoassays for MMP-7 and MMP-8 were also developed. Research projects on the mechanisms of MT1-MMP inhibition by TIMP-2 and expression of TIMP-1,2,3,4 in osteoarthritic and rheumatoid arthritic cartilages are now under way.

Research Products (20 results)

All | Other

All | Publications (20 results)

[Publications] Ohuchi E.: "A ono-step sandwich enzyme immunoassay for human matrix metallo-proteinase 7 (matrilysin) using monoclonal antibodies." Clin. Chim. Acta. 244. 181-198 (1996)

[Publications] Nakamura S.: "Enhancement of SPARC/osteonectin synthesis in articular cartilage. Its increased levels in synovial fluids from patients with rheumatoid arthritis and regulation by growth factors and cytokines in chondrocyte cultures." Arthritis Rheum.39. 539-551 (1996)

[Publications] Ohuchi E.: "Membrane-type l-matrix metalloproteinase digests interstitial collagens and other extracellular matrix macromolecules." J. Biol. Chem.272. 2446-2451 (1997)

[Publications] Imai K.: "Degradation of decorin by matrix metalloproteinases. Identification of the cleavage sites, kinetic analyses and transforming growth factor-βl release." Biochem. J.(in press). (1997)

[Publications] Okimura A.: "Cartilage-matrix protein (CMP) synthesis is enhanced in arthritic cartilage." Arthritis Rheum.(in press). (1997)

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[Publications] Nagase H.: "Proteinases and matrix degradation. Textbook of Rheumatology" W. B. Saunders Com., Philadelphia, 1904 (1997)

[Publications] Ohuchi E., Azumano I., Yoshida S., Iwata K.and Okada Y.: "A one-step sandwich enzyme immunoassay for human matrix metalloproteinase 7 (matrilysin) using monoclonal antibodies." Clin.Chim.Acta. 244. 181-198 (1996)

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[Publications] Nagase H.and Okada Y.: "Proteinases and matrix degradation. In Textbook of Rheumatology." Ed.by Kelley W.N., Harris E.D., Jr., Ruddy S.and Sledge C.B.5th edition, W.B.Saunders Company.Philadelphia. 323-341 (1997)

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Published: 1999-03-08