Expression of enzymic protein and mRNA of proteinases 
in synovial tissue of rheumatoid arthritis

Takashi Sawai, Miwa Uzuki, Hiromi Shiwaku and Ryo Ichinohasama
Department of Pathology, Tohoku University School, Sendai, Japan

Many kinds of proteinases have been said to play an important role in the deterioration of joints in rheumatoid arthritis. However, we knew little about the cells responsible for synthesizing and retaining these enzymes. Recently by in situ hybridization, we have become to be able to detect mRNA related production of enzymic protein.

In this study we investigated the expression of protein and mRNA of several kinds of proteinases to detect the kinds of enzymes participating in tissue destruction in rheumatoid arthritis.

Materials and Methods:

Synovial tissues of RA patients examined in this study were obtained during surgery for total knee replacement and were fixed in 4 % paraformaldehyde in PBS for 1 hour at room temperature, then embedded in paraffin. Three micron sections were used in an immunohistochemical study with avidin-biotin complex and in situ hybridization analysis based on Hayashi's method.

Antibodies used in this study were as follows; anti-stromelysin and -collagenase antibodies (supplied by M. Kurkinnen), -cathepsin B, H, L antibodies (supplied by Dr.Ii), -cathepsin D antibody (purchased from Novocastra Lab. Ltd).

The cDNA of stromelysin and collagenases used for in situ hybridization were kindly supplied by Dr. M. Kurkinnen of UMDNJ, Robert Wood Johnson medical School, U.S.A.

Results and discussion:

In synovial tissues, both enzymic protein and mRNA of stromelysin and collagenase were expressed strongly in the synovial cells located in the superficial layer. However, only a few kinds of cells such as endothelial, muscle cells of small vessels and so called “interstitial cells” with elongated cytoplasm, weakly expressed these enzymes in deeper layer. On the other hand, cathepsin B, H, L and D were expressed not only in the synovial cells located in the superficial layer but also in fibroblastic cells, macrophages and the so-called interstitial cells throughout the whole synovia.
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Next, in granulation tissues around the deteriorated cartilage, cathepsin B, H, L and D were expressed in various kinds of cells in the granulation tissue (pannus), while stromelysin and collagenase were expressed in chondrocytes, losing the proteoglycan matrix around them, and were not detected in the granulation tissues either by immunohistochemical or in situ hybridization methods. The results suggest that optimal conditions and sites for the expression of the proteinases, that is to say, stromelysin and collagenase belonging to neutral proteinases are expressed in the superficial layer and the degraded chondrocytes, while asparatic proteinases such as cathepsin D and cysteine proteinases such as cathepsin B, H, L were expressed in the active inflammatory lesion. The cathepsin enzymes play a more important role in tissue destruction than the metalloproteinases.

Fig.1: Stromelysin protein (left) and mRNA (right) of stromelysin are expressed in the B synoviocytes located in the superficial layer.

Fig.2: Cathepsin D protease is expressed in the many kinds of cells in the granulation tissue (pannus) around the deteriorated cartilage.

References: