THU0067 ANALYSIS OF AUTOANTIGENS RECOGNISED BY AUTOANTIBODIES THAT IMMUNOPRECIPITATE HIGH MOLECULAR WEIGHT NUCLEIC ACIDS

¹M Suzuki, ¹M Hirakata, ¹A Suwa, ¹T Nojima, ¹H Yasuoka, ¹S Satoh, ¹T Fujii, ²S Inada, ³T Mimori. ¹Internal Medicine, Keio University School of Medicine; ²Division of Rheumatic Disease, Tokyo Ohtsuka Metropolitan Hospital, Tokyo; ³Clinical Immunology, Kyoto University, Kyoto, Japan

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Background A number of sera from patients with connective tissue diseases that immunoprecipitated high molecular weight (hwm) nucleic acid smear have been found in RNA-immunoprecipitation (IPP) assay. Most of these sera are supposed to contain autoantibodies for DNA- or mRNA- (or its precursor) related proteins. However, neither the characteristics of antigens nor the clinical significance have been well-defined.

Objectives To analyse the corresponding antigens for autoantibodies immunoprecipitating hwm-nucleic acid smear and to elucidate the clinical features associated with these autoantibodies.

Methods We examined 63 sera from patients with various kinds of connective tissue diseases that immunoprecipitated hwm nucleic acid smear by RNA-IPP. IPP using [35S] methionine-labelled HeLa cell extracts was performed for analysis of the protein components. Immunoprecipitated nucleic acid components were treated with DNase I or RNase A to identify either DNA or RNA.

Results DNA and a heterodimer of 70 kDa and 80 kDa proteins (p70/p80) that was identified as the Ku antigen, was immunoprecipitated by 16 patient sera (4:SLE, 7: myositis overlap syndrome, 1: interstitial pneumonia (IP), 4: undiagnosed). In addition, DNA-protein complex consisting of four polypeptides (11 kDa-21 kDa) that appeared to be histone core proteins, was immunoprecipitated by 18 sera (12:SLE including one drug-induced lupus, 5:MCTD/overlap syndrome, 1: autoimmune hepatitis). Eight patients sera (5:SLE, 2:RA, 1:IP) reacted with the 140 kDa protein along with hwm-RNA smear that was supposed to be RNA helicase A. It should be noted that the remaining 37 of 63 (59%) patients sera immunoprecipitated none of proteins with defined specificities, but various unidentified proteins.

Conclusion Autoantibodies to the Ku, histone, and RNA-helicase A have been identified in patients sera with SLE and other rheumatic diseases that immunoprecipitated hwm-nucleic acid smear. However, a high percentage of these sera were found to contain novel hwm nucleic acids-related antibodies. Further analysis of these autoantibodies may provide clues for understanding the pathogenic mechanism of connective tissue diseases.

Background Disc degeneration and physiopathology of disc herniation involves enzymatic processes mainly matrix metalloproteinases (MMPs), tissue inhibitor of metalloproteinase-1 (TIMP-1) and cytokines (IL-1b, TNF-a).

Objectives This study focuses on metalloproteinases secretion and expression by disc chondrocytes isolated from herniated and not herniated zone.

Methods Eleven discs after discectomy are enzymatically digested, chondrocytes from both zones, herniated and not herniated, are cultured in alginate beads for 10 days in classical conditions. Analysis of MMP-2,-3,-7,-9,-13 and TIMP-1 by ELISA, zymography, RT-PCR and nested PCR are conducted with an immunochemical study on tissue fragments.

Results - proteic level: (ELISA, zymography):

?presence of elevated levels of MMP-3, TIMP-1 in the non herniated part

?absence of MMP-13, MMP-9, pro MMP-7 in both parts

-Transcriptional level (RT, PCR, nested PCR):

?expression of MMP-2, -3, TIMP-1 in both zones, weak expression of MMP-9 by nested PCR without difference between the two zones.

?absence or weak expression of MMP-13, -7.

Conclusion There is an heterogeneous expression of MMP -2, -3, -9 and TIMP-1 by disc herniated and non herniated chondrocytes. The matrix metalloproteinases are probably involved early in the disc degeneration, the herniation could be the final result of matrix/cells interactions.

The secretion of TIMP-1 and MMP-3 in the herniated zone may be related discal fibrosis included into the disc cicatrization.

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AB0019 EFFECT OF EXTRACELLULAR SODIUM CONCENTRATION IN BIGLYCAN AND DECORIN SYNTHESIS BY HUMAN CHONDROCYTES

¹IA Ferraz-Amaro, ¹E Trujillo, ²MF Arteaga, ²I Cozar, ²J Avila, ¹S Bustabad, ¹T Gonzalez, ²P Martin-Vasallo. ¹Servicio de Reumatología; ²Departamento de Biología Y Bioquímica Molecular, Universidad de La Laguna, La Laguna, Spain

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Background An altered chondrocytes phenotypic expression of biglycan and decorin is an early event in osteoarthritis (OA). Changes in extracellular matrix sodium concentration ([Na⁺]) occurs in OA. Previous results suggested that chondrocytes are sensitive to changes in their extracellular [Na⁺] environment and respond with variations in the matrix synthesis.

Objectives Here we have studied the influence of extracellular [Na⁺] on the metabolism of small proteoglycans, biglycan and decorin, in a human chondrocyte-like cell line, C20/A4.

Methods Extracellular deposition of biglycan and decorin was analysed in C20A4 cells cultured: 1) immunohistochemically using specific antibodies against biglycan and decorin and

Cartilage in bone biology and pathophysiology

AB0018 INTERVETEBRAL DISC HERNIATION: INVOLVEMENT OF METALLOPROTEINASES

¹L Grange, ¹P Gaudin, ²JJ Favre, ³M Peoc'h, ¹R Juvin, ¹X Phelip, ²JP Chirossel, ⁴F Morel. ¹Departement of Rheumatology; ²Departement of Neurosurgery; ³Departement of Pathology, Chu, Albert Michallon, Grenoble University Teaching Hospital, Grenoble, France; ⁴Grep JE. EA 2019 MENRT (Groupe de Recherche Et D'Etude Du Processus Inflammatoire)

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