NEW SERUM BIOMARKER FOR RHEUMATOID ARTHRITIS

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Introduction. Development of hypercellular invasive pannus tissue within synovial joints is a hallmark of Rheumatoid Arthritis (RA). Pannus produces proteases that damage bone and cartilage. Non-invasive monitoring of pannus activity is important for clinical assessment of patients as well as for control of the efficacy of therapeutic interventions. Available biomarkers are not satisfactory in terms of pannus specificity and sensitivity for monitoring local inflammation and bone erosion. Our goal is collecting clinical samples of synovial fluid and plasma from patients with RA and/or osteoarthritis (OA) to study the role of WNT signaling in pannus formation and developing set of serum biomarkers to monitor pannus activity.

Materials and methods. Upon collaboration with rheumatologists from the Republican Diagnostic Center (RDC, Astana), we examine existing and new RA and OA patients to establish and confirm their clinical diagnosis. MRI of knee joints, X-ray analysis of inflamed wrists, hematological complete blood counts of cellular components, analyses for C-reactive protein, rheumatoid factor and anti-citrullinated protein antibodies are performed along with complete medical examination. Synovial fluid is withdrawn, and primary cultures of adherent synoviocytes are established. Collagen Triple Helix Repeat-containing 1 (CTHRC1) protein levels are measured by ELISA.

Results and discussion. Synoviocyte primary cultures were established from five OA and six RA patients. Cultures show a distinct morphology and cell proliferation characteristics. Heparinized vein blood plasma was prepared from nine RA and nine OA patients, and from three healthy individuals. ELISA for CTHRC1 demonstrated significantly higher level of the protein in RA patients (average plasma level 23 ng/ml, synovial 22.7 ng/ml) when it was compared to OA (average plasma level 0.8 ng/ml, synovial 0.1 ng/ml). Difference between RA and OA was notable both for plasma and for synovial fluid (28.9 folds and 227 folds, respectively). Healthy plasma was completely negative for CTHRC1.

Conclusions. We demonstrated that ELISA has appropriate sensitivity to detect CTHRC1 in biological fluids. Preliminary analysis showed notably higher plasma and synovial levels of CTHRC1 protein, a member of non-canonical WNT pathway. These results indicate that CTHRC1 can be used as a new serum biomarker for pannus activity in RA. The marker is instrumental for the differential diagnosis of RA and OA versus normal samples.

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