

The Characterization of B Cell Populations in Patients with Rheumatoid Arthritis Focused to B Lymphocytes Specific for Citrulline Containing Peptides

The objective of this study was to investigate the distribution of peripheral blood B cell subpopulations and to analyze the presence of B lymphocytes specific for citrulline containing proteins in peripheral blood and synovial tissue of patients with rheumatoid arthritis (RA) compared with healthy controls and patients with other rheumatic diseases.

The immunophenotyping was performed by polychromatic flow cytometry. Five biotinylated citrulline containing peptides derived from natural proteins were used. Single-cell RT-PCR was employed to analyze expressed V_H gene families.

A significant reduction in frequencies of circulating memory B cells was found, which suggests a selective migration of these cells into inflamed tissue. B lymphocytes specific for at least two of used peptides were detected in all of analyzed peripheral blood and synovial tissue samples. The frequencies of $CD19^+$ B lymphocytes specific for citrulline containing proteins were higher in synovial tissue compared to peripheral blood, the increase was statistically significant for peptide P1 (filaggrin). The identical immunoglobulin rearrangements were found in individual B cells isolated from synovial tissue of a patient with RA.

In conclusion, these data indicate the presence of several B cell subsets specific for different citrulline containing autoantigens in patients with RA and point to the role of anti-CCP autoantibody producing cells in the development of the disease. The higher frequencies of citrullinated peptide specific B lymphocytes in synovial tissue compared to peripheral blood and their clonal relation in synovial tissue suggest the autoantigen driven selection and activation of B cells ongoing directly in the inflamed joint.

Klíčová slova:

revmatoidní artritida, B lymfocyty, proteiny obsahující citrulin, CD antigeny, V_H přestavba, klonalita, plazmatické buňky, průtoková cytometrie, single-cell RT-PCR

Key words:

rheumatoid arthritis, B lymphocytes, citrulline containing proteins, CD antigens, V_H rearrangment, clonality, plasma cells, flow cytometry, single-cell RT-PCR