

Autoantibodies targeting G-protein-coupled receptors in RA and SLE

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Introduction: Previous studies have suggested a role of autoantibodies against G-protein-coupled receptors (GPCR) in autoimmune diseases. In this study, we aimed to determine the association of anti-GPCR autoantibodies with RA and SLE.

Methods: The discovery cohort consisted of 10 patients with rheumatoid arthritis (RA), 10 patients with systemic lupus erythematosus (SLE), and 10 sex- and age-matched healthy donors (HD). Serum levels of autoantibodies against 14 GPCRs were measured for the discovery cohort by ELISA (Celltrend, Germany). Autoantibodies with significant difference between patients and controls were further investigated in a validation cohort containing 40 patients with RA, 14 patients with SLE, and 40 HD. For autoantibodies confirmed in the validation cohort, bioinformatic analysis was performed to explore possible functional interactions among them, and their diagnosis values were evaluated by ROC analysis.

Results: For RA, levels of autoantibodies against 8 GPCRs were significantly different between patients and controls, 7 of which were confirmed in the validation cohort, including C5aR, C3aR, CXCR3, CXCR4, M3R, β 1-adrenergic receptor and AT1R. For SLE, levels of autoantibodies against 2 GPCRs, β 2-adrenergic receptor and ETAR, were significantly different between patients and controls, both were confirmed in the validation cohort. For the autoantibodies that were significantly changed in RA patients, bioinformatic analysis revealed that they were functionally related to chemotaxis. The ROC analysis showed good diagnostic values for all of those autoantibodies which were significantly changed in RA or SLE compared with controls.

Conclusion: Levels of autoantibodies against GPCRs are significantly changes in RA and SLE compared to healthy controls, suggesting that they might be associated with the development of diseases.