Revision November 2023 // Version 1

Human

WHITE PAPER

Autoantibodies against RA33 and diagnosis of rheumatoid arthritis

The best treatment success of rheumatoid arthritis (RA), a chronic inflammatory autoimmune disease, is achieved if the disease is diagnosed at an early stage. The disease manifests in swollen and tender joints and if left untreated, RA can lead to synovial joint destruction, severe disability, and premature mortality. RA occurs with a prevalence of about 0.5% in all global regions and all ethnic groups. Latest diagnostic classification criteria of the American College of Rheumatology and the European League against Rheumatism (ACR/EULAR, 2010) are optimized for early disease detection combining a mixture of physiological examination and laboratory analysis. Swollen joints are the initial criterium. If less than 10 joints are affected, a positive serologic finding is mandatory to diagnose RA.

Autoantibodies are part of the ACR criteria, and rheumatoid factor (RF) as well as anti-citrullinated peptide antibodies (ACPA) are evaluated, as. autoantibodies can precede any clinical manifestation by many years. Routine lab-diagnostics are mostly limited to these both types of autoantibodies. So called seronegative samples refer to these two parameters, but do not exclude the presence of further autoantibodies which still might point to RA as for instance anti-RA33. A study showed that in patients with low or negative RF anti-RA33 occurred in 14% of RA patients with low overlap to anti-CCP.

Anti-RA33 antibodies are anti-nuclear antibodies directed against the A2 protein of the heteronuclear ribonucleoprotein complex (hnRNP-A2). Autoantibodies against the 33 kDa protein were first described in patients with rheumatoid arthritis, leading to the name RA33. In first reports anti-RA33 antibodies have been found in approximately 36% of patients affected by RA.
Anti-RA33 serves as an additional marker in several systemic autoimmune rheumatic diseases (SARD). Various global studies show the benefit of anti RA33 detection. In a Russian cohort anti-RA33 autoantibodies have been found in 11.8% of SARD patients compared to 1.1% of healthy controls. Amongst those about 15% of RA patients, 10% with spondyloarthropathy, 17% with systemic sclerosis and 8% with systemic lupus erythematosus showed elevated anti-RA33 titers. RA33 antibodies additionally serve as well as a marker for the SLE subtype with erosive arthritis. A further enhancement for the diagnosis is shown as RA patients respond to RA33 but not to snRNPs. Also, studies have shown that anti-RA33 antibodies have been associated with a mild disease in RA. They were detected almost exclusively in early RA and identified patients with low radiographic erosion scores, showing potential as a prognostic marker.

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