Autoantibodies play a role in disease development in systemic lupus erythematosus (SLE). Titers of ds DNA antibodies can be used to diagnose SLE and evaluate disease activity.

**What is SLE?**

Systemic lupus erythematosus (SLE) is a systemic (affecting multiple organs and systems) autoimmune connective tissue disorder that presents with diverse symptoms of variable severity involving inflammation and damage to a variety of different tissues and organs. Although the pathology or disease process in systemic lupus erythematosus remains unclear, autoantibodies, particularly antibodies directed against double stranded (ds) DNA are thought to play a role in disease development and progression.

**Autoantibodies in SLE**

Autoantibodies seen in systemic lupus are directed against nuclear antigens such as nucleosomes, DNA, and histone proteins found within the body's cells and plasma. Autoantibodies are involved in disease development either by forming immune complexes that lodge in target organs, disrupting normal organ function, or by cross-reacting with targeted antigens and damaging tissue. Targets of autoantibodies in SLE include nuclear and cytoplasmic macromolecules, lipid components, and plasma proteins. The most frequently associated autoantibodies in SLE include smith (Sm), nucleosomes, histones, and double stranded (ds) DNA. Anti-ds DNA antibodies are the most frequently detected antibodies in systemic lupus erythematosus.

**ACR Classification**

The American College of Rheumatology (ACR) has developed diagnostic criteria that are used to diagnose systemic lupus. Elevation of anti-nuclear antibodies (ANA) is one of the most sensitive serological findings with more than 95 percent of patients with systemic lupus having an elevated ANA titer at some time during the course of their disease. However, the ANA test is not specific for SLE and positive test results are seen in other connective tissue disorders.

**Anti-ds DNA Antibodies**

One type of ANA, the ds-DNA antibody, which was first described in the 1950s, reacts with double stranded deoxyribonucleic acid (DNA). While antibodies to single stranded (ss) DNA are seen in many rheumatic and non-rheumatic conditions, antibodies to ds DNA are considered diagnostic for SLE. Rising and high titers of ds DNA antibodies suggest an increased risk of progressive disease. However, ds DNA titers frequently decrease during disease flares, likely due to the formation of immune complexes. In immune complexes, autoantibodies bind with antigens and or complement.
Anti ds DNA antibodies are considered responsible for much of the kidney disease and renal manifestations that can occur in SLE. A strong correlation exists between renal disease activity and anti-ds DNA antibody titers and the development of lupus nephritis.

Autoantibody Tests

There are numerous methods available to test for autoantibodies. However, not all testing methods have the same test sensitivity. In the case of anti-ds DNA antibodies, different testing methods detect a different spectrum of antibodies. In general, ELISA methods are the most sensitive followed by the Farr and Crithidia assays. However, the ELISA method is the least specific, which means that other related antibodies could be measured with this assay. The Farr assay is often regarded as the gold standard because of its specificity in detecting ds DNA antibodies. Most laboratories will use a combination of two different assays in an effort to provide a specific and sensitive detection. However, tests performed at different laboratories cannot usually be relied on to detect differences in titer because of these diagnostic challenges.

Resources:


Isenberg D, Smeenk R, Clinical laboratory assays for measuring anti-ds DNA antibodies. Where are we now? Lupus 2002;11:797-800.

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