Anti-double stranded DNA (anti-dsDNA) Antibodies

Background

Between 60% and 80% of patients with systemic lupus erythematosus (SLE) have circulating antibodies to double stranded DNA (dsDNA) at some time during their illness.[1] Their presence provides the clinician with one out of the four American College of Rheumatology (ACR) serologic criteria necessary to classify a patient as having SLE.[2]

The techniques most commonly used for detection of anti-dsDNA antibodies are enzyme linked immunosorbent assay (ELISA), enzyme immunoassay (EIA), indirect immunofluorescence using the haemoflagellate *Crithidia luciliae* (CLIF), and the Farr radioimmunoassay (Farr).[3]

ELISA and CLIF detect anti-dsDNA antibodies with both high or low avidity. As the Farr assay includes ammonium sulphate precipitation at high salt concentrations, a condition that dissociates dsDNA-anti-dsDNA complexes of low avidity,[4] this assay detects only antibodies with high avidity.[5]

High avidity anti-dsDNA antibodies are more specific for SLE than those with low avidity[5] and have high predictive value for the development of SLE if present in patients with manifestations compatible with SLE who fulfill fewer than four ACR criteria at the time of evaluation (lupus-like disease, LLD).[6]

Measuring dsDNA

When it comes to detecting antibodies against dsDNA, several methods can be used, including the Farr method (Euroimmun), CLIF (Euroimmun) and the BioPlex 2200 multiplex bead-based EIA (BioRad). Each method has its own advantages and disadvantages, and the choice of method depends on several factors such as the clinical context, the availability of resources, and the desired sensitivity and specificity.

The Farr assay, considered the gold standard,[7] is a commonly used method for measuring the presence of dsDNA antibodies in biological samples. Compared to other dsDNA antibody detection methods, such as CLIF and BioPlex 2200 multiplex EIA, the Farr method has several advantages.[8,9]

1. The Farr assay is highly specific for dsDNA antibodies, as it uses highly purified, native dsDNA as the antigen. In contrast, the *Crithidia luciliae* assay uses indirect immunofluorescence on an intact, but fixed *Crithidia* parasite, which contains other antigens that can cause false positives. The BioPlex 2200 multiplex EIA uses synthetic circular plasmid dsDNA as the antigen, which may not accurately represent the native structure of folded dsDNA and can result in false positive or negative results.

Clinical Usefulness

- The presence of dsDNA antibodies provides one out of the four serologic ACR criteria necessary to classify a patient as having SLE.[2]
- High avidity anti-dsDNA antibodies are more specific for SLE than those with low avidity[5] and have high predictive value for the development of SLE if present in patients with manifestations compatible with SLE who fulfill fewer than four ACR criteria at the time of evaluation (LLD).[6]
- The Farr assay detects only antibodies with high avidity.[5] It is highly specific for dsDNA antibodies and it has a higher sensitivity than other methods.

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2. The Farr assay has a higher sensitivity than the *Crithidia luciliae* assay. This is because the Farr assay uses radiolabeled dsDNA, which allows for a more sensitive detection method. The BioPlex 2200 multiplex assay uses a fluorescent detection system, which can be less sensitive than a radioactive detection system.

3. The Farr assay is a well-established method that has been used for many years in clinical laboratories. As a result, there is a wealth of information and expertise available on this assay, which can help with interpretation of results and troubleshooting any issues that may arise. The *Crithidia luciliae* and BioPlex 2200 multiplex EIA are relatively newer.

In summary, the Farr assay is a highly specific and sensitive method for detecting dsDNA antibodies and has several advantages over other dsDNA antibody detection methods.

Evaluating different dsDNA assays

Since 1957, when anti-dsDNA antibodies were identified, many different assays have been developed to measure their appearance in patients with autoimmune diseases. They have demonstrated their usefulness in the diagnosis and monitoring of the disease. Notably, the Farr assay is one of the most reproducible anti-dsDNA antibodies detection approaches. However, it uses radioactivity and may miss low avidity antibodies.

The reactivity of sera against the CLIF is very simple and sensitive, but it is a semi-quantitative detection system. Nowadays, immobilized dsDNA on beads is a very easy, safe and rapid quantitative assay (EIA) to be applied in the clinical practice, but it does not detect antibodies to tertiary and quaternary structures of folded dsDNA found in *Crithidia*. The predictive potential of anti-dsDNA antibodies lays on their biological activity and their ability to cause the pathological changes typically found in patients with SLE.[10]

Test Name	Test No.
Anti-dsDNA (Double-stranded) Ab by Farr method (RDL)	520059
Anti-dsDNA Ab by IFA, *Crithidia luciliae*, with Reflex to Titer	096346
Anti-dsDNA (Double-stranded) Antibodies by Multiplex	096339

References

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