Autoantibodies: The mystery revealed

Connective Tissue Diseases

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Anti double-stranded desoxyribonucleic acid (dsDNA): First description in patients with bacterial infections in 1938 then in patients with systemic lupus erythematosus (SLE) in 1957

Anti-dsDNA antibodies

Autoantibodies may recognize single-stranded DNA (ssDNA) or double-stranded DNA (dsDNA):

Antibody	Target
Anti-ssDNA	DNA bases (guanosine, thymidine, adenosine, cytosine)
Anti-ssDNA Anti-dsDNA	Sugar-phosphate backbone of DNA
Anti-dsDNA	dsDNA double helix (β-helical dsDNA, Z-DNA, DNA/RNA hybrids, 'kinked' dsDNA, triplex DNA)

Only anti-dsDNA antibodies have a clinical value

- **Isotype** : Only IgG and IgA correlate with SLE disease activity.
- **Detection techniques:** Crithidia luciliae immune-fluorescent test (CLIFT) ++ or Farr assay is recommended.

Method	Advantages	Limits
FARR (Gold standard)	High specificity ≥ 90% Qualitative	Low sensitivity Radioactive material
CLIFT	High specificity ≥ 90% Qualitative	Low sensitivity
ELISA	High sensitivity Quantitative	Low specificity (71% to 100%) False positive (ssDNA)++

- Other methods : fluorescent/chemiluminescent enzyme immunoassay, and multiple-parameter assays.

Found mainly in: SLE: Sensitivity: 36% - 68% and Specificity >90%

But also:

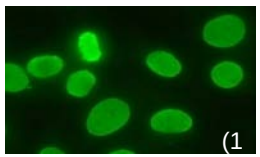
- Autoimmune hepatitis (type 1)

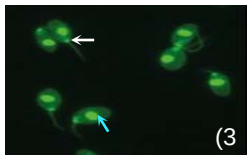
Clinical associations in SLE:

- Weighs 6 points in the ACR/EULAR 2019 classification criteria (detected by an assay with ≥90% specificity)
- Marker of activity => Weighted 2 points in the SLEDAI score if increased more than 25%.
- Associated with **Lupus nephritis** and its activity.

- **IIF pattern on HEp-2 cells (1):** Homogeneous staining of interphase nuclei and condensed chromosomal staining of mitotic cells.
- **CLIFT (2):** Intense fluorescence of the kinetoplast (red arrows), which is rich in dsDNA and poor in histones*.

* Samples are classified as anti-dsDNA negative (3) if the kinetoplasts in the cells do not exhibit fluorescence, regardless of the fluorescence observed in the nuclei (blue arrow) or basal bodies (white arrow).





Anti-dsDNA antibodies should be tested whenever Antinuclear antibodies are positive, regardless of their pattern.

Less than 1% of cases, ANA may be negative while anti-dsDNA are positive

References