Autoantibodies: The mystery revealed

Connective Tissue Diseases

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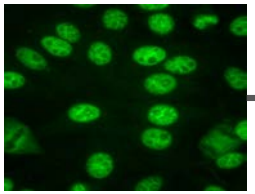
Anti-Ku antibodies

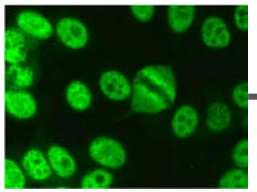
- First described in 1981 in scleroderma–polymyositis overlap syndrome patients
- **Target antigen**: Ku is a DNA-binding protein made up of two subunits (70 kDa and 80 kDa). It plays a crucial role in repairing double-stranded DNA breaks through the non-homologous end-joining pathway. Ku's function and location within the cell change with the cell cycle.

- Found in a wide variety of connective tissue syndromes: IIM, systemic sclerosis, Systemic lupus erythematosus (SLE), Sjögren Syndrome, rheumatoid arthritis, overlap syndromes
- The prevalence of anti-Ku antibodies in connective tissue diseases varies depending on the detection method

- Anti-Ku antibodies are found in about **20%** of idiopathic inflammatory myopathies (IIM)
- Higher prevalence of **interstitial lung disease** in IIM
- Associated to:
  overlap syndromes with muscular involvement
  Raynaud's phenomenon
  muscular involvement
  joint involvement
- Marker of **good response to glucocorticoid treatment**

In SLE:
- Coexistence of anti-dsDNA and anti-Ku abs, increases the risk of lupus nephritis





Screening technique: Indirect immunofluorescence on HEp-2 cells (IIF).

IIF pattern on HEp-2 cells:
- Nuclear fine speckled, nucleoli marked or not
  ⇒ Characteristic appearance, sometimes at higher dilutions.
- perichromatin of cells in mitosis.
- Homogenous (but rarely in isolated anti-Ku)

These patterns are not specific and confirmation techniques are needed.

Confirmation techniques:
- Immunoprecipitation (IP): Gold standard
- Immunoblot (IB): Nuclear antigen profile/ Myositis antigen profile.

⇒ Prevalence varying in sera from patients with overlap syndromes from only 2% when using a highly specific IP method, to 16%–33% by immunoblotting.

- Enzyme-linked immunosorbent assays (ELISAs): safe, rapid, sensitive and specific technique, quantitative results.

Be careful of the potential reactivity of anti dsDNA abs in anti-Ku abs assays.

- Line/dot blot assay
- Chemiluminescence immunoassays (CIAs): high sensitivity and specificity.

References

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