Autoantibodies: The mystery revealed

Connective Tissue Diseases

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Anti-Cyclic Citrullinated Peptide Antibodies (anti-CCP)

- **1979**: detection of **anti-keratin antibodies** in rat esophagus IF in RA patients (sensitivity: 50 - 60% / specificity: 95%)
- **1990**: anti-keratin antibodies recognize in fact **filaggrin molecules**
- **1998**: filaggrin proteins were shown to be **citrulline residues: Citrullination**, a post-translational modification enzymatically mediated by peptidyl arginine deiminase (**PAD**)

Family: Along with anti-SA and anti MCV abs, they form anti-citrullinated protein antibodies (**ACPA**)
ACPA = Anti-CCP abs, + anti-MCV abs + anti-SA abs
⇒ When you use anti-CCP to detect ACPAs**,** almost all ACPAs react. Due to non-cyclic citrulline peptides, the term ACPA is broader than the anti-CCP antibody.

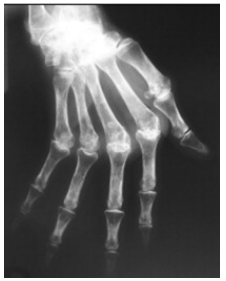
Detection technique:

Immunodetection with marked reagents using mainly **ELISA**. Three generations exist

- **1999**: **CCP1** citrullinated synthetic pro-filaggrin peptide composed of amino acid residues 306-324 of filaggrin
- **2002**: **CCP2** enhanced by screening a library of approximately 12 million synthetic peptides, leading to a peptide specifically optimized for anti-CCP detection.
- **2005**: **CCP3,** designed via combinatorial peptide engineering, presents multiple citrullinated epitopes in a conformational structure, enhancing immunoreactivity.

Rheumatoid arthritis (RA)

- **Sensitivity**: 64 to 79%.
- **Specificity**: greater than 99%.
- Included in the **2010 ACR/EULAR** classification criteria:
  If low titers: 2 points
  If high titers: 3 points
- Also serve as paramount biomarkers for poor prognosis of RA.
- Their remarkable stability, despite fluctuations, and a modest correlation with disease activity make them useless in guiding therapeutic interventions.
- Underscores distinctions in genetic predispositions between anti-CCP positive and anti-CCP negative RA subtypes



But also:

- in **Sjögren's Syndrome** in 1 to 8% of cases, in **Systemic Lupus Erythematosus** in 1%, in **Scleroderma** in 3%, in **hepatitis C associated with cryoglobulinemia** in 7% and in **infections** in 2%
- And in **healthy subjects** in 1% of cases.

References