Autoantibodies: The mystery revealed

Connective Tissue Diseases

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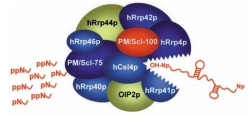
- Firstly described in 1977 in an **overlap syndrome** of systemic sclerosis (SSc) and polymyositis
- **Target antigen:** PM/Scl, a macromolecular complex, recognized as the human **exosome, involved in RNA degradation and processing**



Anti-PM/Scl antibodies

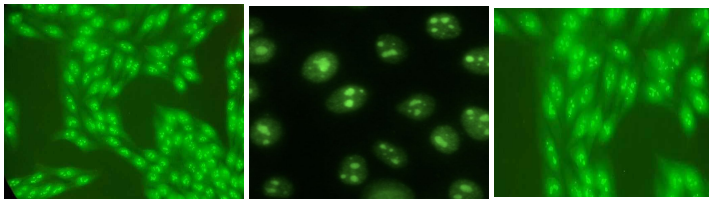
The two main autoantigenic protein components were identified and termed PM/Scl-75 and PM/ Scl-100

Even though the isolated presence of an antigenic specificity is observed in only 3 to 10% of cases, the simultaneous search for these two targets is relevant. Furthermore, some authors suggest specific clinical phenotypes for each antigenic target

Found in 4 to 8% Idiopathic Inflammatory myopathies and in 3% of Systemic sclerosis

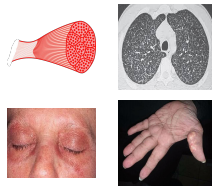
IIF pattern on HEp-2 cells: Homogeneous nucleolar

In addition, Anti-PM/Scl antibodies can yield a weak diffuse nuclear fine speckled staining



Clinical associations and prognosis: Overlap syndrome

- Associated with muscle weakness
- Elevated Creatine Kinase, Interstitial Lung Disease (Non Specific Interstitial Pneumonia pattern)
- DM rash and calcinosis with less pulmonary arterial hypertension and esophageal symptoms.
- Displays a lower death risk compared to other SSc subsets in the first 10 years mainly due to milder ILD progression



Indirect immunofluorescence staining of HEp-2 cells (IIFA) (Gold Standard)

-high sensivity for PM-Scl antibodies
-interference of other anti nucleolar autoantibodies : anti-fibrillarin or anti-RNA polymerase I

multispecific immunoassay

Differentiate between two isotypes of anti-PM/Scl antibodies that may be related to distinct systemic sclerosis (SSc) clinical subsets

Immunoprecipitation

reference standard method : detect antibodies reactive with the native structure of proteins.

monospecific immunoassay

-PM/Scl ELISA
-PM1-Alpha ELISA

line/dot immunoassays

-Often yields false positives due to concurrent SSc-associated ANAs, including anti-topo I, anti-U3 RNP, anti-Ku, and anti-RNA polymerase III antibodies

-False negative are more common with Pm-scl 75

-line/dot immunoassays should not be used in the diagnosis of SSc without corroborative IIF

References