Autoantibodies: The mystery revealed

Connective Tissue Diseases

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Firstly reported in **2010** using immunoprecipitation in patients with myositis features

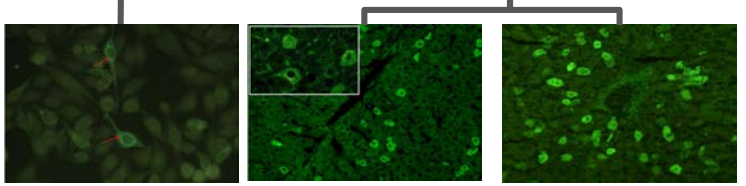
Name: Anti-Hydroxy-3-methyl-glutaryl-Coenzyme A reductase (HMGCR)
Target antigen : An oxidoreductase involved in the mevalonate pathway, rate-limiting step in cholesterol synthesis.
-Located at the membrane of the endoplasmic reticulum
-The pharmacological target of statins.
-Overexpressed in cancer tissues and regenerating muscle cells.

Anti-HMGCR antibodies

Screening technique: Indirect Immunofluorescence

HEp-2 cells
Fine granular cytoplasmic fluorescence with a perinuclear reinforcement on 3% or less of Hep-2 cells, observed in only 35% of patients
⇒ **Currently used substrate**

On kidney/stomach/liver substrates:
Scattered hepatocytes with a centro-lobular distribution. Staining is confined to the cytoplasm and sparses clearly the nuclei.
Less than 10% of the hepatocytes are stained in a given liver lobule.
The bile duct, the endothelium and the cells in the sinusoids are spared.
Stomach and kidney don't show any characteristic pattern



Main disease
Immune-mediated necrotizing myopathy (IMNM)

Proximal muscle weakness with high level of serum creatine kinase (CK)

- Interstitial Lung disease occurs in less than 5%.
- The muscle prognosis in IMNM is typically worse than in other types of myositis
- Abs titers correlate with muscle strength and CK levels but seem to never become negative
- Half of anti-HMGCR myopathy patients continue to have significant weakness after 2 years of treatment.

- Included in the **European Neuromuscular Centre (ENMC) criteria for IMNM (2017)**
- The statin exposure is a risk factor for developing the disease in **40% of patients**
- Cancer risk is higher than in anti-SRP IMNM.
- It's considered intermediate according to ACR

Confirmation techniques

- IP assay: **gold standard**: specificity of ~94–100% and sensitivity of ~95–99%.
- ELISA: sensitivity and specificity: 94.4% and 99.3% respectively.
- These antibodies are detected in 0.7% of healthy subjects by ELISA.
- ALBIA, ELISA and CIA: all three tests showed 100% qualitative concordance

References

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