

## 19 ANTI-RO52 EPI TOPE MAPPING IN INFLAMMATORY MYOPATHIES

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**Background** Specific or associated autoantibodies are present in a majority of patients with idiopathic inflammatory myopathies (IIM). The most frequent myositis associated autoantibodies are directed to Ro52-kd protein (present in

12–26%). Antibodies towards the immunodominant epitope (p200) of Ro52 are associated with neonatal heart block (CHB) in SLE and Sjögren's syndrome (SjS) with the increasing evidence for their pathogenic role. Less is known about possible pathogenic involvement of anti-Ro52 in IIM. Presence of anti-Ro52 in patients with anti-Jo-1 autoantibody is associated with interstitial lung disease (ILD) and suggested decreased survival rate.

**Objective** To investigate possible associations of reactivity to Ro52 epitopes with disease manifestations, autoantibody profile and HLA-DRB1 alleles in myositis. In order to confirm the hypothesis of ongoing epitope spreading with time, the association of disease duration with polyreactivity was evaluated.

**Methods** Serum samples from 468 myositis patients were collected in three countries: Czech (n=133); Hungary (n=202), Sweden (n=133). Antibody specificity against recombinant full length (FL) Ro52 antigen, its four deletion fragments (Ro52-3, -4, -5 and -6) and 7 overlapping synthetic peptides (p136–200) covering the major immunodominant region (Ro52-3) was measured by ELISA. Myositis specific and associated autoantibodies (Jo-1, PL-7, PL-12, EJ, OJ, SRP, PM-Scl, Ku, Mi-2 $\beta$ , U1-RNP) were detected by line-blot immunoassay. 417 patients were genotyped for HLA-DRB1.

**Results** One hundred and eighty-four patients with dermatomyositis (DM), 250 polymyositis (PM), 11 inclusion body myositis, 20 juvenile DM/PM and three with mixed connective tissue disease were included in the analysis. Overlap with other systemic disease (OM) was present in 67 (14%) and ILD in 132 (29%) of patients. Median disease duration was 4.7 (0–41.5) years.

Reactivity to Ro52-FL was present in 97 (21%) samples. Of these, 87 (90%) patients showed specificity to Ro52-3. Within these anti-p176 dominated (66; 76%) compared to anti-p200 in 44 (51%) patients.

Anti-Ro52FL positivity was associated with presence of ILD (OR 3.8;  $p < 0.0001$ ), anti-Jo1 (OR=9.0;  $p < 0.0001$ ) and HLA-DRB1\*03 allele (OR=1.9;  $p = 0.009$ ). No significant epitope associations were detected. The reactivity to 2 or more peptides was associated with OM ( $p = 0.036$ ). No correlation with disease duration was found.

**Conclusion** Our results confirm the association between anti-Ro52 autoantibody positivity with lung involvement, anti-Jo-1 autoantibodies and HLA-DRB1\*03 allele in myositis.

The predominance of reactivity to epitope p176 in myositis patients is different from that which has been reported in patients with SLE and SjS, but the clinical significance is not clear. There was no evidence of epitope spreading in anti-Ro52 response.

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