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A major genetic determinant of autoimmune diseases is associated with the presence of autoantibodies in hypersensitivity pneumonitis

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Alleles from 8.1 ancestral haplotype (#HLA-DRB1 and DQB1 loci) are associated with #autoantibodies production in #hypersensitivity #pneumonitis in a cohort of Mexican mestizo patients https://bit.ly/3bprPeB

Cite this article as: Buendía-Roldán I, Santiago-Ruiz L, Pérez-Rubio G, *et al*. A major genetic determinant of autoimmune diseases is associated with the presence of autoantibodies in hypersensitivity pneumonitis. *Eur Respir J* 2020; 56: 1901380 [https://doi.org/10.1183/13993003.01380-2019].

ABSTRACT

Background: Hypersensitivity pneumonitis is an immune-mediated disease triggered by exposure to organic particles in susceptible individuals. It has been reported that a subgroup of patients with hypersensitivity pneumonitis develops autoantibodies with or without clinical manifestations of autoimmune disease. However, the mechanisms involved in this process and the effect of the autoantibodies on clinical course in hypersensitivity pneumonitis is unknown. We evaluated the association between human leukocyte antigen (HLA) class II alleles and hypersensitivity pneumonitis patients with and without autoantibodies.

Methods: 170 hypersensitivity pneumonitis patients were included. We analysed the presence of antinuclear antibodies, rheumatoid factor, anti-SSA/Ro, anti-SSB/La and anti-CCP at the time of diagnosis. In addition, in a subset of patients we evaluated anti-Scl-70, anti-neutrophil cytoplasmic antibody, and anti-DNA. HLA typing was performed using PCR sequence-specific primers in a high-resolution modality, including *HLA-DRB1* and *HLA-DQB1* loci. Statistical analysis was performed employing Epi-Info v7 and SPSS v20.

Results: 60 hypersensitivity pneumonitis patients showed sera autoantibodies ($HPAbs^+$), and 110 hypersensitivity pneumonitis patients did not ($HPAbs^-$). The frequency of the allele *HLA-DRB1*03:01* was remarkably increased in the $HPAbs^+$ group (10.8% *versus* 0.45%; OR 30.14, 95% CI 3.83–237.1; $p=1.65\times10^{-4}$ after Bonferroni's correction). Likewise, we found that the haplotype *DRB1*03:01-DQB1*02:01*, which is part of the 8.1 ancestral haplotype, a major genetic determinant of autoimmune diseases, confers significant risk to develop autoantibodies (OR 19.23, 95% CI 2.37–155.9; p=0.0088 after Bonferroni's correction). In addition, the *HLA-DRB1*03:01* allele was associated with higher mortality in patients with hypersensitivity pneumonitis (adjusted OR 5.9, 95% CI 1.05–33.05; p=0.043).

Conclusions: A subset of hypersensitivity pneumonitis patients presents circulating autoantibodies and higher mortality that are associated with some alleles of 8.1 ancestral haplotype.