

Comparing HLA shared epitopes in French Caucasian patients with scleroderma.

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Objective. To test whether ⁶⁷FLEDR⁷¹, a common amino acid sequence, shared by HLA-DRB susceptibility alleles in scleroderma (SSc), or ⁷¹TRAE⁷⁷ a common amino acid sequence shared by HLA-DQB1 susceptibility alleles, is a better prognostic marker for SSc. Furthermore, FLEDR is either expressed on the β 1 chain of HLA-DR11 molecules or on the β 5 chain of HLA-DR15 molecules. As β 5 chain is often considered as under expressed, we asked whether FLEDR motif would be underrepresented when carried by DR β 5 chains (in HLA-DR15 molecules) compared to DR β 1 (in HLA-DR11 molecules).

Methods. Allelic HLA-DRB and DQB typing was performed for a total of 468 healthy controls and 282 patients with SSc allowing FLEDR and TRAE⁷⁷ analyses. Results were stratified according to patient's clinical subtypes and autoantibody status. Standardized HLA-DR β 1 and DR β 5 reverse transcriptase Taqman PCR assays were developed to quantify β 1 and β 5 chain mRNA in 20 subjects with HLA-DRB1*15 and/or DRB1*11 haplotypes.

Results. FLEDR motif is highly associated with diffuse SSc ($\chi^2=34.5$, $p<10^{-6}$) and particularly in patients with anti-topoisomerase antibodies ($\chi^2=53.4$, $p<10^{-9}$) whereas TRAE⁷⁷ association is weaker in both subgroups ($\chi^2=7.2$, $p=0.027$ and ($\chi^2=14.7$, $p=0.0006$ respectively). Furthermore, in HLA-DR15 molecules, β 5mRNA is more expressed than β 1mRNA chain.

Conclusions. In French Caucasians, FLEDR epitope is highly associated with scleroderma patients with anti-topoisomerase antibodies. Moreover, FLEDR is always carried by the most abundantly expressed β chain: β 1 on HLA DR11 and β 5 on HLA-DR15 haplotype, suggesting a determinant presentation role.