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Evaluation of Systemic Sclerosis Risk Genes in the Turkish Population

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Session Time: 9:00AM-11:00AM

Background/Purpose: The use of high-throughput genotyping platforms has allowed a better understanding of the genetic background underlying systemic sclerosis (SSc). Sixteen non-HLA genes have been consistently associated with SSc at the genome-wide level of significance, with *IRF5*, *STAT4*, *CD247*, *DNASE1L3*, *IL12A* and *ATG5* representing the top signals in the two most powered large-scale analyses on SSc performed to date (a genome-wide association study and an Immunochip study in Europeans). We aimed to evaluate for the first time the possible role of the above mentioned genes in SSc susceptibility in the Turkish population.

Methods: We genotyped a total of 355 SSc patients and 718 unrelated healthy controls from Turkey for the SSc-associated lead genetic variants *IRF5* rs10488631, *STAT4* rs3821236, *CD247* rs2056626, *DNASE1L3* rs35677470, *IL12A* rs77583790, and *ATG5* rs9373839. The genotyping of the whole SSc group and part of the control group (219 samples) was performed by TaqMan assays, whereas the remaining control data (499 samples) was obtained using the Immunochip platform. To test for association, we compared the minor allele frequencies of every polymorphism between cases and controls by performing 2×2 contingency tables and x2 tests.

Results: The overall analysis evidenced statistically significant associations of the global SSc with *IRF5* (P=1.48E-05, OR=1.76, CI 95%=1.36-2.27) and *CD247* (P=2.20E-03, OR=0.75, CI 95%=0.62-0.90). Trends of association were also suggested for *STAT4* (P=0.066, OR=1.21, CI 95%=0.99-1.48), *IL12A*

(P=0.080, OR=4.06, Ci 95%=0.74-22.23), and *DNASE1L3* (P=0.100, OR=1.41, CI 95%=0.93-2.11). Interestingly, the subphenotype analysis showed subtype- and autoantibody-specific associations, that is, *CD247* was specifically associated with the diffuse form of the disease (diffuse SSc vs controls: P=4.91E-04, OR=0.64, CI 95%=0.49-0.82; diffuse SSc vs limited SSc: P=0.065, OR=0.75, CI 95%=0.55-1.02), and *IRF5* with the presence of anti-topoisomerase autoantibodies (ATA+ SSc vs controls: P= 8.84E-08, OR=2.28, CI 95%=1.68-3.11; ATA+ SSc vs ATA- SSc: P=8.43E-03, OR=1.70, CI 95%=1.14-2.52).

Conclusion: We were able to replicate the associations of *IRF5* rs10488631 and *CD247* rs2056626 with SSc in the Turkish population, thus confirming the relevant role that these genes may have in the pathophysiology of this disease.

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