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Analysis of the genetic component of systemic sclerosis in Iranian and Turkish population through a genome-wide association study

David González-Serna¹, Elena López-Isac¹, Neslihan Yilmaz², Farhad Gharibdoost³,
Ahmadreza Jamshidi³, Hoda Kavosi³, Shiva Poursani³, Faraneh Farsad⁴ Haner Direskeneli⁵,
Guhre Saruhan-Direskeneli⁶, Amr H. Sawalha⁷, Matthew A. Brown⁸, Sule Yavuz²,
Mahdi Mahmoudi³ and Javier Martin^{1*}

¹Institute of Parasitology and Biomedicine López-Neyra, Consejo Superior de Investigaciones Científicas, Granada, Spain

²Department of Rheumatology, Istanbul Bilim University, Istanbul, Turkey

³Rheumatology Research Center, Tehran University of Medical Sciences, Tehran, Iran

⁴Department of Rheumatology, Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

⁵Division of Rheumatology, Marmara University, Istanbul, Turkey

⁶Department of Physiology, Istanbul Medical Faculty, Istanbul University, Istanbul, Turkey

⁷Division of Rheumatology, Department of Internal Medicine, University of Michigan, and the Center for Computational Medicine and Bioinformatics, University of Michigan, Michigan, USA

⁸Institute of Health and Biomedical Innovation, Queensland University of Technology, Translational Research Institute, Princess Alexandra Hospital, Queensland, Australia

*Corresponding author: Javier Martin. Institute of Parasitology and Biomedicine López-Neyra, Consejo Superior de Investigaciones Científicas, Granada, Spain. E-mail: javiermartin@ipb.csic.es

Abstract

Objectives. Systemic sclerosis (SSc) is an autoimmune disease characterized by alteration of the immune response, vasculopathy and fibrosis. Most genetic studies on SSc have been performed in European-ancestry populations. The aim of this study is to analyze the genetic component of SSc in Middle Eastern patients from Iran and Turkey through a genome-wide association study (GWAS).

Methods. This study comprises a total of 834 patients diagnosed with SSc and 1,455 healthy controls from Iran and Turkey. DNA was genotyped using high-throughput genotyping platforms. The data generated were imputed using the Michigan Imputation Server and the Haplotype Reference Consortium (HRC) as reference panel. A meta-analysis combining both case/control sets was conducted by the inverse variance method.

Results. The highest peak of association belonged to the HLA region in both the Iranian and Turkish populations. Strong and independent associations between the classical alleles *HLA-DRB1*11:04* ($p=2.10 \times 10^{-24}$, OR=3.14) and *DPB1*13:01* ($p=5.37 \times 10^{-14}$, OR=5.75) and SSc were observed in the Iranian population. *HLA-DRB1*11:04* ($p=4.90 \times 10^{-11}$, OR=2.93) was the only independent signal associated in the Turkish cohort. An omnibus test yielded HLA-DRB1 58 and HLA-DPB1 76 as relevant amino acid positions for this disease. Concerning the meta-analysis, we also identified two associations close to the genome-wide significance level outside the HLA region, corresponding to *IRF5-TNPO3* rs17424921-C ($p=1.34 \times 10^{-7}$, OR=1.68) and *NFKB1* rs4648133-C ($p=3.11 \times 10^{-7}$, OR=1.47).

Conclusions. We identified significant associations in the HLA region and suggestive associations in *IRF5-TNPO3* and *NFKB1* loci in Iranian and Turkish patients affected by SSc through a GWAS and an extensive HLA analysis.

Keywords: Systemic sclerosis; GWAS; Iranian and Turkish populations; risk loci.

Key messages:

- HLA region is strongly associated with SSc susceptibility in Iranian and Turkish populations.
- *IRF5-TNPO3* and *NFKB1* loci showed suggestive association in both populations.
- *GOT1-NKX2.3* emerged as a new potential susceptibility locus in SSc.

Introduction

Systemic sclerosis (SSc) is an uncommon autoimmune disease with high mortality and morbidity, characterized by altered immune response, vascular damage and abnormal fibrosis of skin and internal organs (1). SSc etiology is complex but, similar to most autoimmune conditions, it is thought that a combination of environmental and a multiplicity of genetic factors lead to its development (2). The disease is clinically classified into two main groups: the limited cutaneous form (lcSSc) and the diffuse cutaneous form (dcSSc). SSc is also characterized by production of specific autoantibodies, being anti-centromere antibody (ACA) and anti-topoisomerase antibody (ATA) (anti-Scl-70) the two most common autoantibodies (1).

Large genetic studies, including genome-wide association studies (GWASs) and Immunochip analyses, have confirmed the human leukocyte antigen (HLA) class II region as the most significant genetic region associated with SSc (3-6) and its different clinical and serological features (5, 6). In addition, it has been evidenced the significant genetic component of non-HLA region in SSc with a total of 14 non-HLA loci showing association at the genome-wide level of significance (p -value $<5.0 \times 10^{-8}$) to date (3-12). However, most of the previous GWASs and HLA analyses for SSc have been performed in European-descent populations. Therefore, the study of the genetic component in different ethnic groups could help to identify unknown, or pinpoint known, disease-associated susceptibility alleles, taking advantage of differences in linkage disequilibrium (LD) structure or allele frequencies between populations.

Thus, we decided to perform the first GWAS for SSc in Iranian and Turkish population. Even though Turkish genetic structure is unique, genetic overlap with the rest of

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3 Middle East population is clearly defined (13). As the HLA region is the most significant
4 genetic association reported for SSc, we also decided to perform an extensive analysis
5 of the HLA region.
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11 **Material and Methods**

12 **Study population**

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16 A series of 834 patients diagnosed with SSc (547 from Iran and 287 from Turkey) and
17 1,455 unaffected and unrelated controls (830 from Iran and 625 from Turkey) were
18 included in this study. All case samples fulfilled the American College of Rheumatology
19 classification criteria for SSc (14). Written informed consent was obtained from all the
20 participants. The study was approved by local ethical committees from the different
21 participant centers, in accordance to our institution (Spanish Research Council) ethical
22 committee, and with the Helsinki Declaration of 1975, as revised in 1983.
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29 Clinical information regarding subtypes of SSc defined by LeRoy *et al* (15), and
30 presence of ACA and ATA were collected. The clinical information was selected based
31 on previous genetic studies determining specific associations with SSc subtypes or
32 autoantibodies status (**Supplementary Table S1**).
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39 **Genotyping**

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42 Genomic DNA was extracted from saliva samples or whole blood by standard methods.
43 The GWAS genotyping of the SSc cases and controls was performed as follows: the
44 Iranian and Turkish SSc cases, together with 136 Turkish controls were genotyped
45 using the Illumina Infinium HumanCore-12v1 BeadChip. The remaining Turkish controls
46 were genotyped using the Illumina HumanOmni1-Quad v1 BeadChip. The control
47 group from Iran was genotyped using the Illumina Infinium CoreExome-24 BeadChip.
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Quality control

We applied the same QC criteria for both the Iranian and the Turkish GWAS data. Single-nucleotide polymorphisms (SNPs) and subjects with call rates lower than 98% and 95%, respectively, were removed using PLINK V.1.9 (16). SNPs with minor allele frequencies (MAFs) lower than 0.01 and those that were not in Hardy-Weinberg equilibrium (HWE; p -value $<$ 0.001) were also excluded. In addition, one subject per duplicate pair and per pair of first-degree relatives was also removed via the Genome function in PLINK V.1.9 with a Pi-HAT threshold of 0.4. Principal component (PC) analyses were performed to identify and exclude outliers based on their ethnicity by using PLINK V.1.9, and the GCTA64 and R-base under GNU Public license V.2. We calculated the 10 first PCs using approximately 100,000 quality-filtered independent SNPs. Those subjects showing more than six standard deviations (SD) from the cluster centroids were considered as outliers. After QC, 764 SSc patients (505 from Iran and 259 from Turkey) and 1,343 controls (770 from Iran and 573 from Turkey) were included in the analysis. A total of 242,501 and 186,435 genotyped SNPs remained after QC filtering of the Iranian and Turkish data sets, respectively (**Supplementary Table S1**).

Imputation of GWAS data

Imputation was performed using the Michigan Imputation Server (MIS) (17). The software SHAPEIT (18) was used in order to estimate the haplotypes, and the European panel in the Haplotype Reference Consortium (HRC) r1.1 (19) was used as reference population for both Turkish and Iranian genotyped data. Imputation was carried out in individual chunks of 50,000 Mb covering whole-genome regions with a probability threshold for merging genotypes of 0.9, to maximize the quality of imputed variants. Imputed data were also subjected to the above mentioned QC filters in PLINK V.1.9. A total of 6,313,908 and 5,885,622 SNPs were finally analyzed in the Iranian and Turkish GWASs, respectively (**Supplementary Table S1**).

Human leukocyte antigen (HLA) imputation

Considering the previous reported strong HLA association with SSc, a more extensive analysis of the HLA region was conducted in Turkish and Iranian cohorts. We extracted the extended major histocompatibility complex (MHC) region (29,000,000 to 34,000,000 bp in chromosome 6) from the non-imputed data and imputed a total of 424 classical HLA alleles at two- and four-digits, 7,261 SNPs and 1,276 polymorphic amino acids. We used the SNP2HLA method with the Beagle software package (20) and a reference panel collected by the Type 1 Diabetes Genetics Consortium composed of 5,225 individuals of the European origin (21). Alleles and amino acids with call rates <95%, and SNPs in deviation from HWE (p -value<0.001), were removed using PLINK V.1.9.

Statistical analyses

The statistical analyses were performed with PLINK and R. First, the Iranian and the Turkish cohorts were independently analyzed by logistic regression on the best-guess genotypes (>0.9 probability) assuming an additive model and including the first 10 PCs as covariates. Odds ratios (ORs) and 95% confidence intervals were calculated according to Woolf's method. Genomic-inflation factor (λ) was estimated at 1.02 in both the Iranian and the Turkish cohorts (Q-Q plot, **Supplementary Figure S1**). We also performed stratified analysis considering the different clinical and serological features (dcSSc, lcSSc, ACA⁺SSc and ATA⁺SSc). Subsequently, the Iranian and the Turkish GWAS data sets were combined by inverse variance weighted fixed effects meta-analysis to integrate the two different association studies. Cochran's Q and I^2 tests were used to measure the heterogeneity of the ORs across studies. SNPs showing association p -values <5.0×10⁻⁸ were regarded as significant. The presence of independent effects was examined using a stepwise logistic regression by conditioning on the lead SNP and the first 10 PCs.

To determine the influence of the polymorphic amino acid positions on disease susceptibility, an omnibus association test (22) was carried out in the Iranian and the

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3 Turkish cohorts as described (23). A null generalized linear model was established,
4 including the 10 first PCs as covariates. Next, an alternative model, including the same
5 variables and all the possible alleles in the analyzed amino acid positions was built.
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7 Finally, to compare both models a likelihood ratio test was conducted.
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13 Results

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15 Following QC and imputation, a total of 5,698,748 SNPs in 764 SSc patients (505 from
16 Iran and 259 from Turkey) and 1,343 controls (770 from Iran and 573 from Turkey)
17 were analyzed.
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21 As shown in **Figure 1**, a high association peak corresponding to the HLA class II region
22 reached the GWAS significance threshold (5×10^{-8}) in both the Iranian and Turkish
23 cohorts. Specifically, for the Iranian cohort, the top associated signal belonged to the
24 SNP rs9268923 ($p=6.55 \times 10^{-18}$, OR=2.29) (**Figure 1-A**). Out of the HLA region, some
25 suggestive level associations were found, highlighting the *IRF5-TNPO3* (interferon
26 regulatory factor 5-transportin 3) and the *NFKB1* (Nuclear Factor Kappa B Subunit 1)
27 loci (**Table 1**), which represent previously reported susceptibility loci for SSc. The top
28 associated signal for the *IRF5-TNPO3* locus corresponds to the SNP rs17424921
29 ($p=5.28 \times 10^{-5}$, OR=1.64) located in an intergenic region and 5' upstream from *TNPO3*
30 gene. This SNP is in strong LD ($r^2=0.92$) in our data set with rs10488631 ($p=6.15 \times 10^{-5}$,
31 OR=1.62), a previously reported SNP associated to SSc (3, 7) located in the intergenic
32 region between *IRF5* and *TNPO3*. Regarding the *NFKB1* locus, the top associated SNP
33 was the rs4648133 ($p=1.52 \times 10^{-5}$, OR=1.48) located in an intronic position. Interestingly,
34 this SNP is in moderate LD ($r^2=0.73$) with rs1598859 ($p=6.23 \times 10^{-3}$, OR=1.27), a
35 previously reported SNP associated to SSc which is located in an intronic position of
36 the *NFKB1* gene (9).
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50 In the Turkish cohort (**Figure 1-B**), the top associated SNP corresponding to the HLA
51 class II region was rs34297496 ($p=9.46 \times 10^{-9}$, OR=2.16). Out of the HLA region, one
52 signal corresponding to the SNP rs7095491 reached the suggestive level of significance
53 ($p=5.17 \times 10^{-7}$, OR=1.88). This SNP is located in an intergenic region between *GOT1*
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3 (glutamic-oxaloacetic transaminase 1) and *NKX2.3* (NK2 Homeobox 3). This locus was
4 specifically associated in the Turkish cohort and did not reach the suggestive level of
5 significance in either the Iranian cohort ($p=3.14E-02$, OR=0.89) or the meta-analysis
6 ($p=3.21E-01$, OR=1.07).
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10 11 12 13 **Meta-analysis**

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15 We decided to perform a meta-analysis in order to identify susceptibility loci to SSc
16 which comprise moderate effect sizes in the Iranian and the Turkish cohorts,
17 independently. The HLA class II region was the highest association peak observed in
18 the meta-analysis (**Figure 1-C**), and the top associated signal belonged to the SNP
19 rs28746976 ($p=1.41 \times 10^{-23}$, OR=2.09). Out of the HLA region, two signals corresponding
20 to the *IRF5-TNPO3* and *NFKB1* loci almost reached the genome-wide significance
21 threshold (**Table 1**). The top associated signals corresponded to the same SNPs
22 observed in the Iranian cohort for both loci, *IRF5-TNPO3* rs17424921 ($p=1.34 \times 10^{-7}$,
23 OR=1.68) and *NFKB1* rs4648133 ($p=3.11 \times 10^{-7}$, OR=1.47) (**Supplementary Figures S2-3**).
24 Non-HLA loci showing genome-wide significant associations ($p < 5 \times 10^{-8}$) were reported
25 for their associations in our data sets (**Supplementary Table S2**).
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38 **HLA analysis**

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40 In order to extensively analyze the association of the HLA region and SSc in both the
41 Iranian and the Turkish populations, a comprehensive HLA imputation was performed.
42 As stated above, a strong association signal was observed within the HLA class II region
43 in both the Iranian and the Turkish GWAS data sets (**Table 2**). Regarding the Iranian
44 cohort, the top associated signal belonged to the classical allele *HLA-DRB1*11:04*
45 ($p=2.10 \times 10^{-24}$, OR=3.14). After controlling for *HLA-DRB1*11:04*, an independent
46 secondary effect was found in the HLA-DPB1 region. Specifically, the top associated
47 signal was the *HLA-DPB1*13:01* ($p=5.37 \times 10^{-14}$, OR=5.75), and no additional
48 independent associations were observed after conditioning on both signals,
49 *DRB1*11:04* and *DPB1*13:01* (**Figure 2**). Significant insights were found in the ATA⁺SSc
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3 vs. controls stratified analysis, as a stronger association between the *HLA-DRB1*11:04*
4 and the disease was evident ($p=2.49 \times 10^{-34}$, OR=4.92). In addition, after controlling for
5 this classical allele, the *HLA-DPB1*13:01* also showed a stronger association
6 ($p=6.44 \times 10^{-21}$, OR=10.60) (**Supplementary Table S3**). We also performed a stratified
7 analysis comparing ATA⁺SSc vs. ATA⁻SSc, showing a strong association of the *HLA-*
8 *DRB1*11:04* with ATA⁺SSc ($p=2.69 \times 10^{-14}$, OR=5.06). After conditioning on *HLA-*
9 *DRB1*11:04*, the *HLA-DPB1*13:01* also showed statistically significant association with
10 ATA⁺SSc ($p=5.02 \times 10^{-8}$, OR=10.21). In the Turkish cohort, *DRB1*11:04* ($p=4.90 \times 10^{-11}$,
11 OR=2.93) showed the most significant association, and no independent secondary
12 effects were found after controlling for this HLA classical allele (**Figure 3**). All
13 statistically significant HLA associations (classical alleles, amino acid variants and SNPs)
14 found in the Iranian and the Turkish HLA analyses are summarized in **Supplementary**
15 **Table S4**.

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26 Subsequently, specific amino acid positions that could be responsible for the
27 association observed for these classical alleles were examined by means of an omnibus
28 test. The most relevant amino acid positions for disease risk in the Iranian cohort were
29 the positions 58 ($P_{LRT}=6.24 \times 10^{-24}$) and 67 ($P_{LRT}=5.76 \times 10^{-22}$) of the HLA-DRβ1 molecule
30 (**Table 3**), which were in strong LD ($r^2=0.83$). After conditioning on the strongest
31 association (position 58), position 76 ($P_{LRT}=1.57 \times 10^{-13}$) of the HLA-DPβ1 protein
32 remained independently associated. None of the other signals remained significant
33 after conditioning on positions 58 and 76 of the HLA-DRβ1 and HLA-DPβ1 molecules,
34 respectively. The most associated amino acid residues for the previously mentioned
35 positions were Glu ($p=5.39 \times 10^{-22}$, OR=2.57) and Phe ($p=1.08 \times 10^{-20}$, OR=2.38) in
36 positions 58 and 67 of the HLA-DRβ1 molecule, respectively, and Ile ($p=1.52 \times 10^{-12}$,
37 OR=4.60) in position 76 of the HLA-DPβ1 (**Supplementary Table S4**). In the case of the
38 Turkish cohort, the position 58 of the HLA-DRβ1 molecule was the only signal reaching
39 the significance threshold ($P_{LRT}=4.96 \times 10^{-8}$) (**Table 3**), being Ala the most associated
40 amino acid residue in that position ($p=9.42 \times 10^{-8}$, OR=2.13). All statistically significant
41 amino acid positions found in the Iranian and the Turkish cohorts are summarized in
42 **Supplementary Table S5**.

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Discussion

This study represents the first GWAS of SSc performed in Iranian and Turkish populations. Given the relevance of the HLA region in SSc predisposition, and the lack of information of the role of HLA genes in SSc in Iranian or Turkish population, we performed an extensive analysis of the HLA region, identifying the HLA class II region as the most strongly associated loci to SSc in both Middle Eastern populations.

Interestingly, we observed that the *HLA-DRB1*11:04* classical allele showed the most significant associations in both populations. Our data reinforce the role of *HLA-DRB1*11:04* allele in susceptibility to SSc in different ethnic populations including Caucasians (24-26), African-Americans (24) and Mexicans (27). Furthermore, our results suggest for the first time that this effect could be driven by the amino acid Glu-58. Nevertheless, amino acid Phe-67, which is in high LD with Glu-58 in our study, has been previously set as a relevant amino acid in susceptibility to SSc (5). After conditioning on *HLA-DRB1*11:04*, the classical allele *HLA-DPB1*13:01*, which has been reported as a susceptibility allele in Caucasians (24) and Koreans (28), remains significant in the Iranian cohort. Our results also suggest that the association between *HLA-DPB1*13:01* and SSc could be driven by the amino acid Ile-76, which is in line with previous results (5). Furthermore, amino acid 76 is part of the binding pocket of the HLA-DPβ1 molecule (29). However, associations of *HLA-DRB1*11:04* and *HLA-DPB1*13:01* with SSc were explained by its strong correlation with ATA in previously mentioned studies. This specific correlation with ATA⁺SSc was verified in our stratified analysis. In this sense, the presence of *HLA-DRB1*11:04* and *HLA-DPB1*13:01* classical alleles specifically associated to ATA in the non-stratified analysis could be owing to a clinical predominance of ATA⁺SSc patients in the Iranian population. On the other hand, the lack of association of *HLA-DPB1*13:01* in the Turkish cohort could be due to the lower sample size as compared to the Iranian cohort.

Outside of the HLA region, two suggestive associations at *IRF5-TNPO3* and *NFKB1* loci were found. *IRF5-TNPO3* was one of the first associated locus identified in SSc and has been replicated in different studies and ethnicities (3-7, 30, 31), representing a firm susceptibility factor for SSc and other autoimmune diseases such as systemic lupus erythematosus and rheumatoid arthritis (32, 33). On the other hand, *NFKB1* locus was

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3 associated as a susceptibility gene in SSc in a GWAS meta-analysis and a subsequent
4 candidate gene approach analysis in Caucasian population (9, 34). NF- κ B has been
5 broadly described to control the inflammatory process and its role in autoimmunity is
6 widely accepted (35). Furthermore, the interaction of *NFKB1* with other well defined
7 susceptibility genes in SSc such as *TNFAIP3* (Tumor Necrosis Factor Inducible Protein
8 A20) (36), which encodes a protein that inhibits NF- κ B activation, suggest that it could
9 be a good candidate gene to be involved in SSc. Regarding the Turkish cohort, a
10 suggestive level associated signal corresponding to the *GOT1-NKX2.3* locus emerged.
11 This locus is a well-established associated signal in other immune-mediated diseases,
12 such as ulcerative colitis or Crohn's disease (37, 38), suggesting a potential role of the
13 *GOT1-NKX2.3* locus in autoimmunity. Furthermore, the strongest association reported
14 for the *GOT1-NKX2.3* locus in both studies (rs4409764) is in strong LD ($r^2=0.93$) with
15 the top associated SNP observed in our Turkish cohort (rs7095491).
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26 Despite the successful identification of SSc susceptibility genes in Iranian and Turkish
27 population, our study has some limitations. In this regard, larger cohorts could help to
28 elucidate if the two suggestive associations observed in meta-analysis (*IRF5-TNPO3*
29 and *NFKB1*) reach the genome-wide significance threshold. Nevertheless, the results in
30 four of the six most relevant SSc hits outside the HLA obtained by Carmona *et al* (39) in
31 Turkish population were closely similar to our GWAS results (**Supplementary Table**
32 **S6**), highlighting the reproducibility of our study.
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In summary, our results confirm previous reports of association of the HLA region with
SSc susceptibility as well as two associations almost reaching the significance threshold
out of the HLA region in Iranian and Turkish populations. This study sheds light on the
unexplored genetic background of SSc in these populations, which contributes to a
better understanding of genetic structure and pathogenesis of the disease.

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Disclosure statement

The authors declare no conflict of interests.

Figure legends

Figure 1. Manhattan plot of the GWAS results from the Iranian cohort (A), Turkish cohort (B) and meta-analysis (C).

The values on the y-axes denote the $-\log_{10}$ transformed p -values. Genomic position for each SNP for 22 autosomes are plotted on the x-axis. The red line denotes the a priori threshold for genome-wide significance ($p = 5 \times 10^{-8}$). The suggestive level of significance ($p = 1 \times 10^{-5}$) is highlighted in blue.

Figure 2. Manhattan plot representation of the results of the conditional logistic regression analysis of the HLA region in Iranian patients with SSc.

(A) Unconditioned test of the HLA region. (B) Results after conditioning on the *HLA-DRB1*11:04* classical allele. (C) Results after conditioning on the *HLA-DRB1*11:04* and *DPB1*13:01*. The red/green color gradient represents the effect direction of each analyzed variant (red for risk and green for protection). The size of the diamonds indicates the degree of linkage disequilibrium with the classical allele *HLA-DRB1*11:04* and *DPB1*13:01* in A and B, respectively. The red line represents the genome-wide level of significance ($p = 5 \times 10^{-8}$).

Figure 3. Manhattan plot representation of the results of the conditional logistic regression analysis of the HLA region in Turkish patients with SSc.

(A) Unconditioned test of the HLA region. (B) Results after conditioning on the *HLA-DRB1*11:04* classical allele. The red/green color gradient represents the effect direction of each analyzed variant (red for risk and green for protection). The red line represents the genome-wide level of significance ($p = 5 \times 10^{-8}$).

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Figure 1.

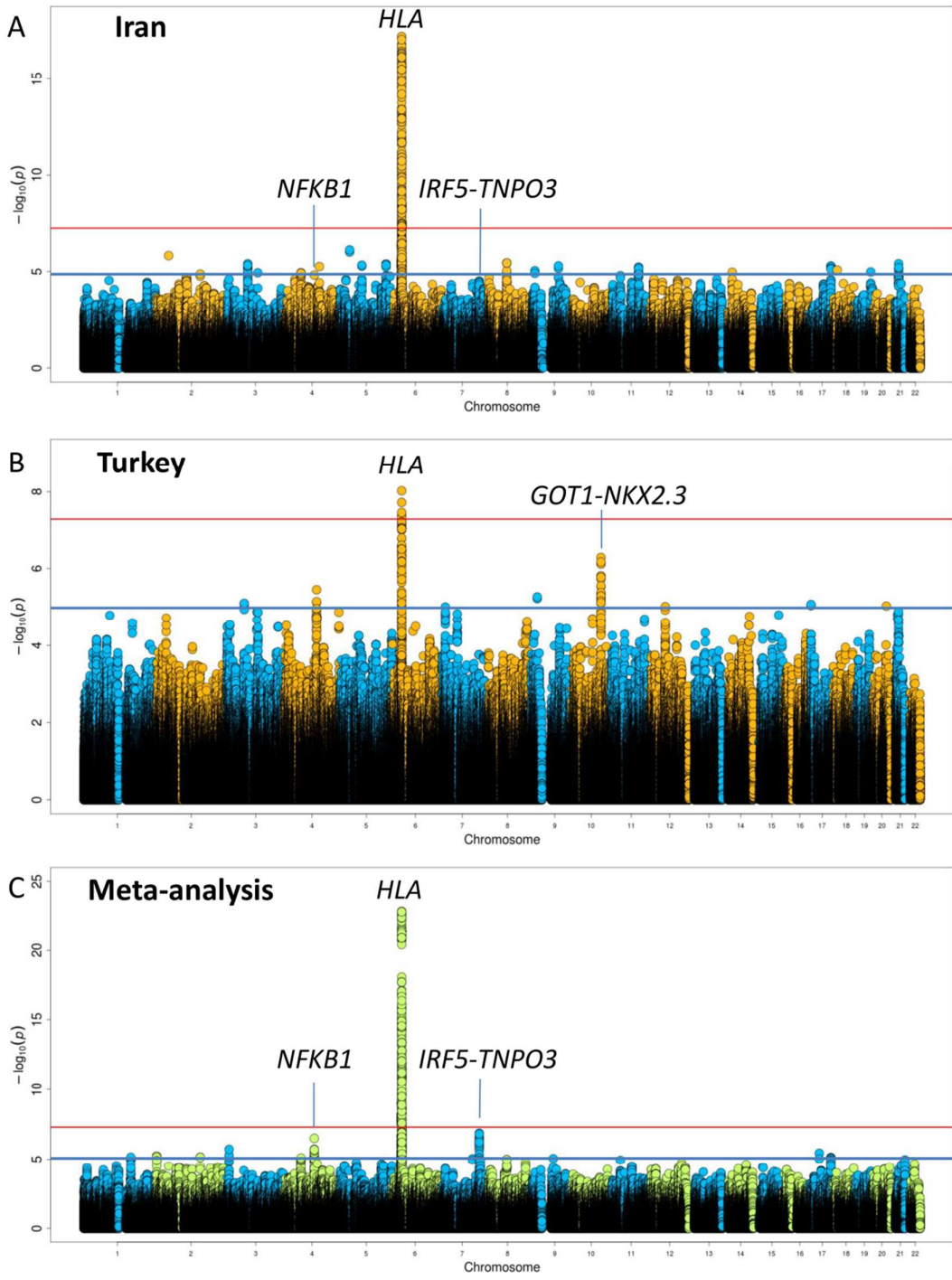
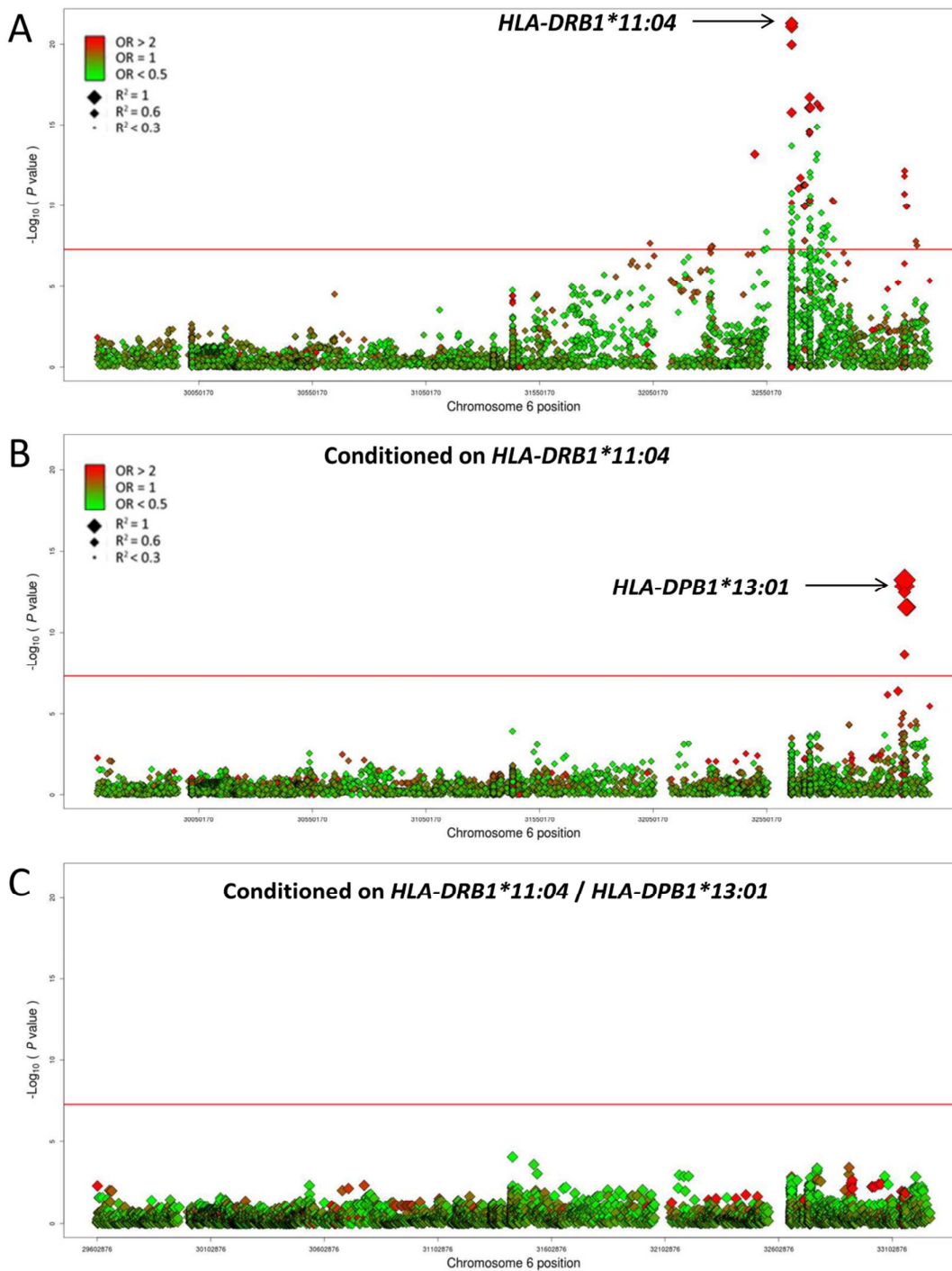
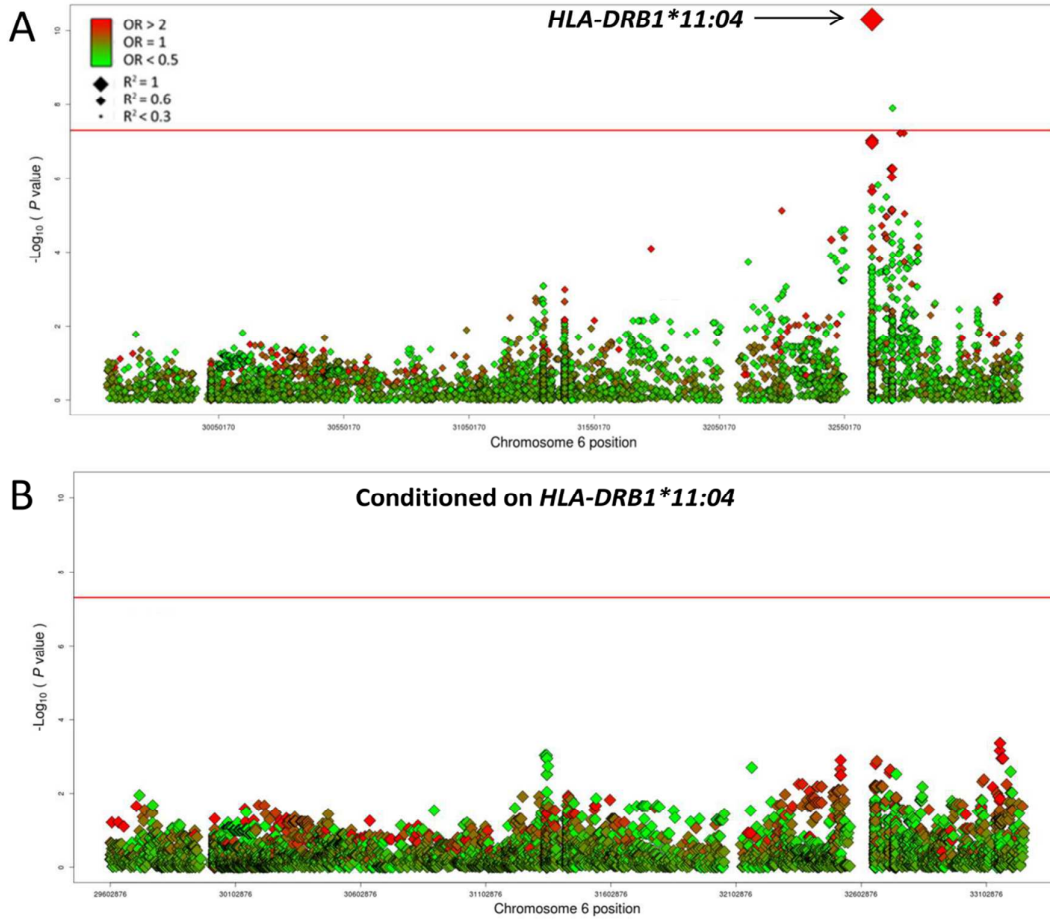


Figure 2.



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Figure 3.



Tables

Table 1. Non-HLA loci associated with SSc at the suggestive significance level ($p < 1 \times 10^{-5}$) in the meta-analysis.

*BP corresponding to the NCBI build 37.

Abbreviations: BP: base pair; Chr: chromosome; SNP: single nucleotide polymorphism; OR: odds ratio; CI: confidence interval; Q and I^2 : heterogeneity values.

Loci	Chr	BP*	Most significant SNP	Minor allele	Iran		Turkey		Meta-analysis			
					p value	OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	Q	I^2
<i>IRF5-TNPO3</i>	7	128708122	rs17424921	C	5.28×10^{-5}	1.64 (1.29-2.08)	6.57×10^{-4}	1.77 (1.27-2.46)	1.34×10^{-7}	1.68 (1.39-2.03)	0.69	0
	7	128594183	rs10488631	C	6.15×10^{-5}	1.62 (1.28-2.05)	3.05×10^{-3}	1.66 (1.18-2.33)	6.35×10^{-7}	1.63 (1.34-1.97)	0.90	0
<i>NFKB1</i>	4	103536413	rs4648133	C	1.52×10^{-5}	1.48 (1.24-1.77)	6.29×10^{-3}	1.45 (1.11-1.89)	3.11×10^{-7}	1.47 (1.27-1.70)	0.90	0
<i>GRM7-LOC101927394</i>	3	7907077	rs9821717	T	2.52×10^{-5}	0.68 (0.57-0.82)	2.23×10^{-2}	0.74 (0.57-0.96)	1.91×10^{-6}	0.70 (0.60-0.80)	0.59	0
<i>UNC45B</i>	17	33501644	rs12452554	C	3.77×10^{-4}	1.74 (1.28-2.35)	2.54×10^{-3}	2.00 (1.28-3.13)	3.57×10^{-6}	1.81 (1.41-2.33)	0.61	0
<i>PXDN-MYT1L</i>	2	1785659	rs2059413	C	2.29×10^{-4}	0.71 (0.60-0.85)	8.01×10^{-3}	0.70 (0.54-0.91)	5.70×10^{-6}	0.71 (0.61-0.82)	0.92	0
<i>LOC101929282-RBM43</i>	2	151773679	rs917238	G	1.73×10^{-5}	1.54 (1.27-1.88)	9.15×10^{-2}	1.28 (0.96-1.72)	6.86×10^{-6}	1.45 (1.23-1.71)	0.30	6.49
<i>ATF6-OLFML2B</i>	1	161937892	rs3002626	A	7.41×10^{-4}	0.73 (0.60-0.87)	2.38×10^{-3}	0.65 (0.50-0.86)	6.98×10^{-6}	0.70 (0.60-0.82)	0.52	0
<i>HOPX-SPINK2</i>	4	57558089	rs9968446	A	1.21×10^{-5}	1.44 (1.22-1.70)	1.46×10^{-1}	1.21 (0.93-1.56)	7.92×10^{-6}	1.37 (1.19-1.57)	0.25	22.08
<i>OSTF1-PCSK5</i>	9	78042927	rs473299	A	1.42×10^{-4}	1.44 (1.19-1.74)	2.02×10^{-2}	1.38 (1.05-1.80)	8.69×10^{-6}	1.42 (1.21-1.65)	0.78	0

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Table 2. Classical four digit HLA alleles showing the strongest association with SSc.

Abbreviations: HLA: human leucocyte antigen; OR: odds ratio; CI: confidence interval.

HLA allele	Iran				Turkey			
	Unconditioned		Conditioned on HLA-DRB1*11:04		Unconditioned		Conditioned on HLA-DRB1*11:04	
	<i>p</i> value	OR (95% CI)	<i>p</i> value	OR (95% CI)	<i>p</i> value	OR (95% CI)	<i>p</i> value	OR (95% CI)
DRB1*11:04	2.10x10⁻²⁴	3.14 (2.52-3.91)	NA	NA	4.90x10⁻¹¹	2.93 (2.12-4.03)	NA	NA
DQB1*03:01	2.04x10 ⁻¹⁷	2.22 (1.84-2.66)	3.08x10 ⁻²	1.31 (1.03-1.68)	9.16x10 ⁻⁷	1.93 (1.49-2.51)	4.51x10 ⁻¹	1.15 (0.80-1.64)
DPB1*13:01	7.23x10⁻¹³	5.05 (3.24-7.86)	5.37x10⁻¹⁴	5.75 (3.65-9.07)	1.79x10⁻³	2.93 (1.49-5.75)	4.48x10⁻⁴	3.43 (1.72-6.84)
DQA1*05:01	1.08x10 ⁻¹⁰	1.77 (1.49-2.11)	6.54x10 ⁻¹	1.05 (0.84-1.31)	1.08x10 ⁻⁵	1.77 (1.37-2.28)	3.46x10 ⁻¹	1.16 (0.85-1.59)

Table 3. Amino acid positions showing the strongest association with SSc after omnibus test.

Abbreviations: HLA: human leucocyte antigen; LRT: likelihood ratio test.

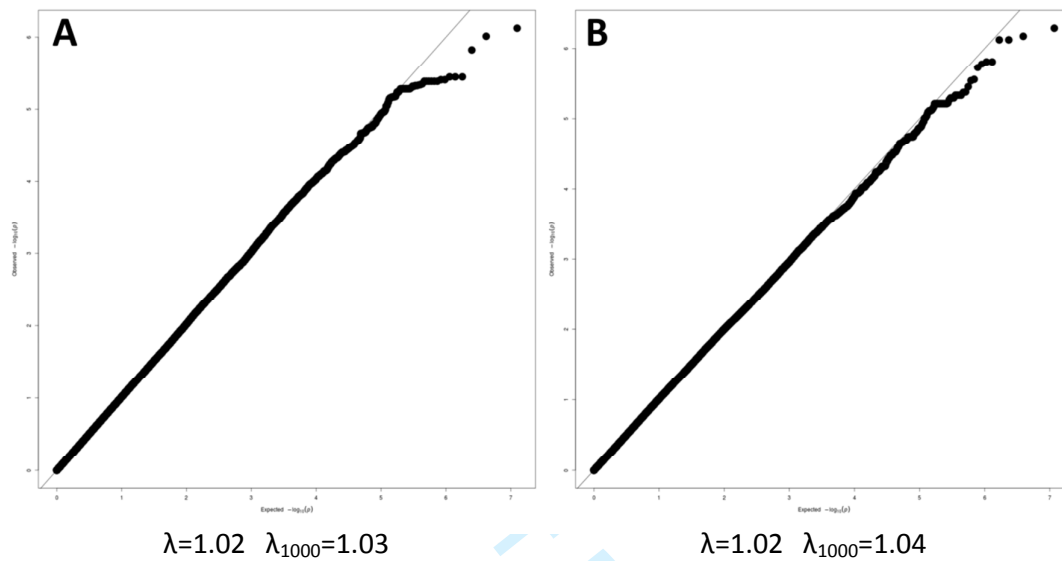
HLA molecule	Amino acid position	Center codon position	Tested Alleles	Iran		Turkey	
				P_{LRT} (unconditioned)	P_{LRT} conditioned on DR β 1 position 58	P_{LRT} (unconditioned)	P_{LRT} conditioned on DR β 1 position 58
DRβ1	58	32659974	2	6.24x10⁻²⁴	NA	4.96x10⁻⁸	NA
DR β 1	67	32659947	3	5.76x10 ⁻²²	4.18x10 ⁻²	6.19x10 ⁻⁶	8.40x10 ⁻¹
DQ β 1	45	32740702	2	1.14x10 ⁻¹⁷	4.67x10 ⁻¹	3.68x10 ⁻⁷	4.15x10 ⁻¹
DQ β 1	55	32740672	3	1.25x10 ⁻¹⁶	1.59x10 ⁻²	6.95x10 ⁻³	2.72x10 ⁻¹
DQ β 1	140	32737868	2	2.47x10 ⁻¹⁶	3.68x10 ⁻²	3.97x10 ⁻³	4.05x10 ⁻¹
DQ β 1	182	32737742	2	2.47x10 ⁻¹⁶	3.68x10 ⁻²	3.97x10 ⁻³	4.05x10 ⁻¹
DPβ1	76	33156640	3	8.06x10⁻¹⁴	1.57x10⁻¹³	8.40x10⁻³	3.93x10⁻³

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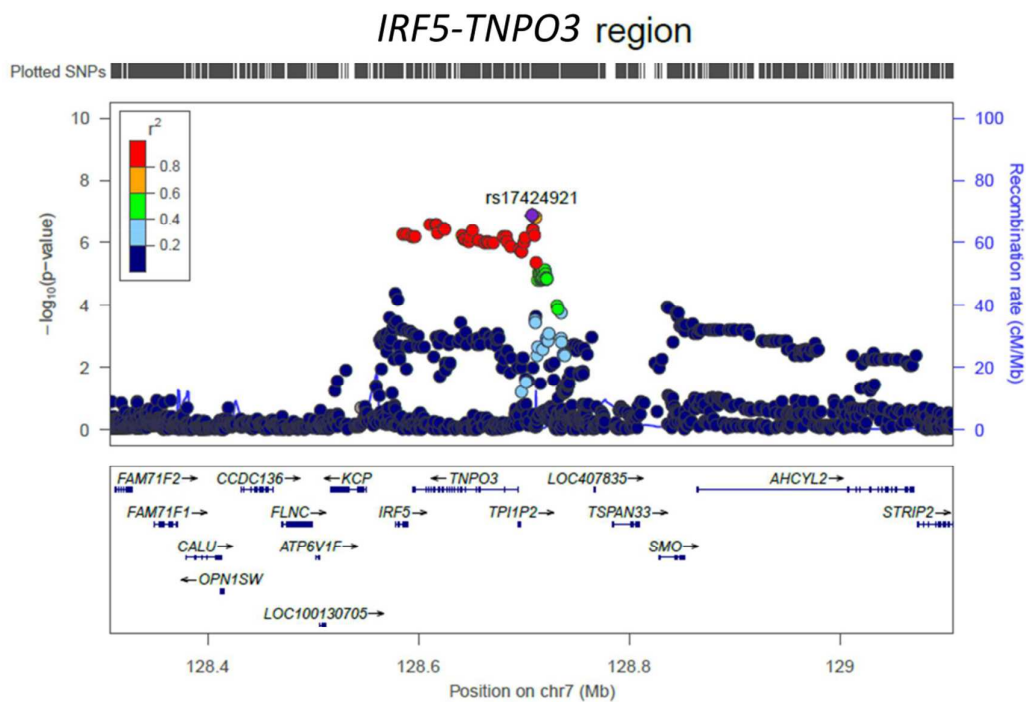
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Supplementary Figures

Supplementary Figure S1. Q-Q (quantile-quantile) plots, excluding the MHC region, for the Iranian (A) and the Turkish (B) cohorts analyses.

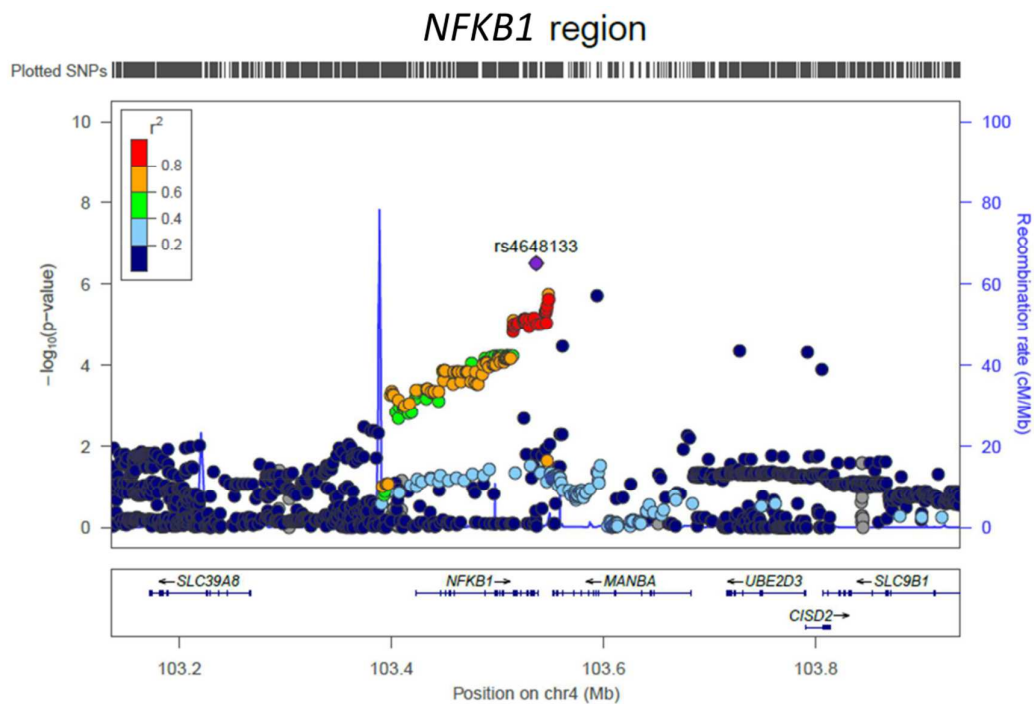


Supplementary Figure S2. Locus zoom plot for *IRF5-TNPO3* region. The p values for association ($-\log_{10}$ values) of each SNP are plotted against their physical position on chromosome 7.



Review

Supplementary Figure S3. Locus zoom plot for *NFKB1* region. The p values for association ($-\log_{10}$ values) of each SNP are plotted against their physical position on chromosome 4.



Review

Supplementary Tables

Supplementary Table S1. Number of subjects and SNPs in the Iranian and Turkish GWASs.

Abbreviations: SSc: systemic sclerosis; dcSSc: diffuse cutaneous systemic sclerosis; lcSSc: limited cutaneous systemic sclerosis; ACA: anti-centromere antibody; ATA: anti-topoisomerase antibody; SNP: single nucleotide polymorphism; QC: quality control.

	Iran		Turkey	
	Before QC	After QC	Before QC	After QC
Number of subjects				
SSc	547	505	287	259
lcSSc	180	165	128	115
dcSSc	301	278	122	111
ACA	30	30	58	47
ATA	384	356	115	102
Healthy Controls	830	770	625	573
Number of SNPs				
Genotyped	279,616	242,501	236,155	186,435
Imputed	8,467,723	6,313,908	7,369,344	5,885,622
Meta-analysis				5,698,748

Supplementary Table S2. The results in the current study for the confirmed non-HLA *loci* associated to SSc at the genome-wide significance level ($p < 5 \times 10^{-8}$) included in our data sets.

*BP corresponding to the NCBI build 37.

Abbreviations: SSc: systemic sclerosis; GWAS: genome-wide association study; Chr: chromosome; BP: base pair; SNP: single nucleotide polymorphism; OR: odds ratio; CI: confidence interval.

Previous reported <i>loci</i>				Minor allele	meta-analysis		Iranian GWAS		Turkish GWAS		References
SNP	Chr	BP*	Gene		<i>p</i> value	OR (95% CI)	<i>p</i> value	OR (95% CI)	<i>p</i> value	OR (95% CI)	
rs3790567	1	67822377	<i>IL12RB2</i>	A	6.65E-01	1.03 (0.73-1.33)	9.40E-01	1.01 (0.84-1.20)	5.18E-01	1.08 (0.68-1.30)	[8]
rs2056626	1	167420425	<i>CD247</i>	G	7.71E-03	0.83 (0.70-0.96)	1.66E-01	0.88 (0.75-1.05)	6.93E-03	0.71 (0.56-0.91)	[3,4,9]
rs7574865	2	191964633	<i>STAT4</i>	T	2.49E-04	1.31 (1.08-1.54)	6.89E-02	1.27 (1.07-1.51)	1.07E-02	1.39 (1.08-1.80)	[3-7,9]
rs2233287	5	150440097	<i>TNIP1</i>	A	7.53E-02	1.22 (0.89-1.55)	2.93E-01	1.15 (0.83-1.50)	1.15E-01	1.34 (0.93-1.93)	[4]
rs9373839	6	106655617	<i>ATG5</i>	C	8.52E-01	0.98 (0.72-1.24)	7.46E-01	0.96 (0.74-1.24)	8.86E-01	1.03 (0.71-1.49)	[5]
rs2230926	6	138196066	<i>TNFAIP3</i>	G	7.67E-01	1.05 (0.66-1.44)	8.31E-01	1.05 (0.68-1.62)	8.35E-01	1.06 (0.59-1.92)	[5]
rs10488631	7	128594183	<i>IRF5-TNPO3</i>	C	6.35E-07	1.63 (1.34-1.97)	6.15E-05	1.62 (1.28-2.05)	3.05E-03	1.66 (1.18-2.33)	[3-7,9]
rs2304256	19	10475652	<i>TYK2</i>	A	3.61E-01	0.93 (0.79-1.07)	1.01E-01	0.85 (0.71-1.03)	4.69E-01	1.10 (0.85-1.43)	[11]
rs2305743	19	18193191	<i>IL12RB1</i>	A	7.88E-02	0.86 (0.65-1.07)	4.12E-01	0.92 (0.75-1.12)	5.20E-02	0.74 (0.54-1.00)	[10]

Supplementary Table S3. HLA classical alleles, SNPs and amino acid variants associated with ATA⁺ systemic sclerosis at the genome-wide significance level ($p < 5 \times 10^{-8}$) in the Iranian cohort. The results of the conditioned analysis are also shown. The marker nomenclature is as follow: 1) Classical HLA alleles: HLA_[gene]_[allele]; 2) HLA amino acids: AA_[gene]_[amino acid position within the molecule]_[genetic position of the center of codon]_[allele]; 3) HLA intragenic SNPs: SNP_[gene]_[genetic position]_[allele]; 4) Insertions/deletions: [variant]_[gene]_[genetic position]_[insertion/x=deletion]. When more than one allele is shown, it refers to the presence of any of them. *For binary encodings, P=present, A=absent.

Variation	Position in Chr 6 (GRCh36)	Allele	Unconditioned		Conditioned on HLA-DRB1*11:04	
			p value	OR (95% CI)	p value	OR (95% CI)
HLA_DRB1_1104	32660042	P	2.49E-34	4.92 (3.81-6.35)	NA	NA
AA_DRB1_58_32659974_A	32659974	A	1.27E-33	4.17 (3.31-5.26)	2.72E-07	2.33 (1.69-3.22)
AA_DRB1_58_32659974_E	32659974	P	1.27E-33	4.17 (3.31-5.26)	2.72E-07	2.33 (1.69-3.22)
SNP_DRB1_32659974_G	32659974	A	1.27E-33	4.17 (3.31-5.26)	2.72E-07	2.33 (1.69-3.22)
SNP_DRB1_32659974_T	32659974	P	1.27E-33	4.17 (3.31-5.26)	2.72E-07	2.33 (1.69-3.22)
HLA_DRB1_11	32660042	P	1.27E-33	4.17 (3.31-5.26)	2.72E-07	2.33 (1.69-3.22)
AA_DRB1_67_32659947_F	32659947	P	6.58E-31	3.59 (2.89-4.46)	2.54E-07	2.06 (1.57-2.72)
SNP_DRB1_32659948_A	32659948	P	6.58E-31	3.59 (2.89-4.46)	2.54E-07	2.06 (1.57-2.72)
HLA_DQB1_0301	32739039	P	2.88E-29	3.58 (2.87-4.48)	6.03E-06	1.94 (1.46-2.59)
SNP_DQB1_32737148	32737148	G	1.08E-28	3.52 (2.82-4.40)	1.44E-05	1.89 (1.42-2.51)
AA_DQB1_45_32740702	32740702	E	1.08E-28	3.52 (2.82-4.40)	1.44E-05	1.89 (1.42-2.51)
SNP_DQB1_32740702	32740702	T	1.08E-28	3.52 (2.82-4.40)	1.44E-05	1.89 (1.42-2.51)
SNP_DQB1_32742309_A	32742309	P	1.08E-28	3.52 (2.82-4.40)	1.44E-05	1.89 (1.42-2.51)
rs5000632	32771666	G	7.77E-28	3.20 (2.60-3.94)	1.44E-07	1.94 (1.52-2.49)
rs9357152	32772938	G	7.77E-28	3.20 (2.60-3.94)	1.44E-07	1.94 (1.52-2.49)
rs9394113	32773145	G	7.77E-28	3.20 (2.60-3.94)	1.44E-07	1.94 (1.52-2.49)
rs9378125	32787710	G	1.41E-27	3.19 (2.59-3.93)	2.00E-07	1.93 (1.51-2.47)
SNP_DRB1_32659973_C	32659973	P	1.55E-26	3.28 (2.64-4.09)	0.0004681	1.67 (1.25-2.24)
HLA_DQB1_03	32739039	P	1.44E-25	3.04 (2.47-3.75)	1.27E-06	1.83 (1.43-2.34)
AA_DQB1_55_32740672_P	32740672	P	1.44E-25	3.04 (2.47-3.75)	1.27E-06	1.83 (1.43-2.34)
SNP_DQB1_32740672_G	32740672	P	1.44E-25	3.04 (2.47-3.75)	1.27E-06	1.83 (1.43-2.34)
SNP_DQB1_32740722	32740722	T	1.44E-25	3.04 (2.47-3.75)	1.27E-06	1.83 (1.43-2.34)
SNP_DQB1_32737124	32737124	A	6.11E-25	2.99 (2.43-3.68)	6.88E-07	1.84 (1.45-2.35)
AA_DQB1_182_32737742_N	32737742	P	6.11E-25	2.99 (2.43-3.68)	6.88E-07	1.84 (1.45-2.35)
SNP_DQB1_32737742	32737742	T	6.11E-25	2.99 (2.43-3.68)	6.88E-07	1.84 (1.45-2.35)
AA_DQB1_140_32737868_T	32737868	P	6.11E-25	2.99 (2.43-3.68)	6.88E-07	1.84 (1.45-2.35)
SNP_DQB1_32737869	32737869	T	6.11E-25	2.99 (2.43-3.68)	6.88E-07	1.84 (1.45-2.35)
SNP_DQB1_32737933	32737933	T	6.11E-25	2.99 (2.43-3.68)	6.88E-07	1.84 (1.45-2.35)
AA_DQB1_182_32737742_S	32737742	A	9.41E-25	2.98 (2.42-3.67)	8.72E-07	1.83 (1.44-2.34)

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AA_DQB1_140_32737868_A	32737868	A	9.41E-25	2.98 (2.42-3.67)	8.72E-07	1.83 (1.44-2.34)
rs5000634	32771542	T	3.65E-24	0.34 (0.28-0.42)	1.22E-07	0.53 (0.42-0.67)
rs7745040	32772310	T	3.65E-24	0.34 (0.28-0.42)	1.22E-07	0.53 (0.42-0.67)
rs3135363	32497626	C	1.29E-23	2.95 (2.39-3.65)	0.00381	1.50 (1.14-1.98)
AA_DQB1_167_32737787_H	32737787	P	2.20E-21	2.69 (2.19-3.30)	0.000947	1.52 (1.19-1.95)
SNP_DQB1_32737787	32737787	T	2.20E-21	2.69 (2.19-3.30)	0.000947	1.52 (1.19-1.95)
AA_DQB1_26_32740759_Y	32740759	P	2.20E-21	2.69 (2.19-3.30)	0.000947	1.52 (1.19-1.95)
SNP_DQB1_32740759_T	32740759	P	2.20E-21	2.69 (2.19-3.30)	0.000947	1.52 (1.19-1.95)
SNP_DQB1_32740760_A	32740760	P	2.20E-21	2.69 (2.19-3.30)	0.000947	1.52 (1.19-1.95)
AA_DQB1_13_32740798_G	32740798	A	2.20E-21	2.69 (2.19-3.30)	0.000947	1.52 (1.19-1.95)
AA_DQB1_13_32740798_A	32740798	P	2.20E-21	2.69 (2.19-3.30)	0.000947	1.52 (1.19-1.95)
SNP_DQB1_32740798	32740798	G	2.20E-21	2.69 (2.19-3.30)	0.000947	1.52 (1.19-1.95)
AA_DQB1_167_32737787_R	32737787	A	3.49E-21	2.68 (2.19-3.29)	0.001149	1.51 (1.18-1.94)
AA_DQB1_30_32740747_Y	32740747	A	7.14E-21	0.36 (0.29-0.45)	9.58E-08	0.53 (0.42-0.67)
SNP_DQB1_32740748_A	32740748	A	7.14E-21	0.36 (0.29-0.45)	9.58E-08	0.53 (0.42-0.67)
AA_DQB1_38_32740723	32740723	V	1.13E-20	0.36 (0.29-0.45)	2.51E-07	0.54 (0.42-0.68)
SNP_DQB1_32740723	32740723	A	1.13E-20	0.36 (0.29-0.45)	2.51E-07	0.54 (0.42-0.68)
SNP_DRB1_32659940	32659940	C	1.21E-20	0.38 (0.31-0.46)	5.52E-05	0.61 (0.48-0.78)
rs6457617	32771829	C	1.45E-20	0.36 (0.29-0.45)	1.26E-06	0.55 (0.44-0.70)
rs6457620	32771977	G	1.45E-20	0.36 (0.29-0.45)	1.26E-06	0.55 (0.44-0.70)
rs9275224	32767856	A	2.03E-20	0.36 (0.29-0.45)	8.32E-07	0.55 (0.43-0.70)
SNP_DQB1_32742296_C	32742296	A	3.22E-20	0.35 (0.28-0.43)	1.03E-07	0.51 (0.40-0.65)
SNP_DQB1_32742309_Cx	32742309	P	5.04E-20	0.39 (0.31-0.47)	8.23E-05	0.62 (0.49-0.79)
SNP_DRB1_32659973_G	32659973	P	5.89E-19	0.40 (0.33-0.49)	8.82E-05	0.63 (0.50-0.79)
rs3129763	32698903	A	2.73E-18	2.45 (2.00-3.00)	0.278	1.16 (0.89-1.52)
HLA_DPB1_13	33157346	P	4.81E-18	7.61 (4.81-12.05)	6.44E-21	10.60 (6.47-17.36)
HLA_DPB1_1301	33157346	P	4.81E-18	7.61 (4.81-12.05)	6.44E-21	10.60 (6.47-17.36)
AA_DPB1_76_33156640_I	33156640	P	5.40E-18	6.97 (4.49-10.82)	9.90E-21	9.66 (6.00-15.55)
AA_DRB1_37_32660037_Y	32660037	P	9.97E-18	2.39 (1.96-2.91)	0.01856	1.34 (1.05-1.70)
SNP_DRB1_32659937	32659937	C	1.06E-17	0.39 (0.32-0.49)	0.0001137	0.62 (0.49-0.79)
AA_DRB1_70_32659938_D	32659938	A	1.06E-17	0.39 (0.32-0.49)	0.0001137	0.62 (0.49-0.79)
SNP_DRB1_32659939	32659939	G	1.06E-17	0.39 (0.32-0.49)	0.0001137	0.62 (0.49-0.79)
rs9272219	32710247	T	1.24E-17	2.40 (1.96-2.93)	0.108	1.23 (0.96-1.59)
SNP_DQA1_32713249	32713249	T	1.24E-17	2.40 (1.96-2.93)	0.108	1.23 (0.96-1.59)
AA_DQA1_40_32717170	32717170	G	1.24E-17	2.40 (1.96-2.93)	0.108	1.23 (0.96-1.59)
SNP_DQA1_32717170	32717170	G	1.24E-17	2.40 (1.96-2.93)	0.108	1.23 (0.96-1.59)
SNP_DQA1_32717190_T	32717190	P	1.24E-17	2.40 (1.96-2.93)	0.108	1.23 (0.96-1.59)
AA_DQA1_47_32717191_C	32717191	P	1.24E-17	2.40 (1.96-2.93)	0.108	1.23 (0.96-1.59)
SNP_DQA1_32717192	32717192	T	1.24E-17	2.40 (1.96-2.93)	0.108	1.23 (0.96-1.59)
AA_DQA1_50_32717200_V	32717200	P	1.24E-17	2.40 (1.96-2.93)	0.108	1.23 (0.96-1.59)
SNP_DQA1_32717201	32717201	T	1.24E-17	2.40 (1.96-2.93)	0.108	1.23 (0.96-1.59)
SNP_DQA1_32717202	32717202	C	1.24E-17	2.40 (1.96-2.93)	0.108	1.23 (0.96-1.59)
AA_DQA1_51_32717203	32717203	L	1.24E-17	2.40 (1.96-2.93)	0.108	1.23 (0.96-1.59)
SNP_DQA1_32717207	32717207	A	1.24E-17	2.40 (1.96-2.93)	0.108	1.23 (0.96-1.59)
SNP_DQA1_32717208	32717208	C	1.24E-17	2.40 (1.96-2.93)	0.108	1.23 (0.96-1.59)
AA_DQA1_53_32717209_Q	32717209	P	1.24E-17	2.40 (1.96-2.93)	0.108	1.23 (0.96-1.59)

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3	SNP_DQA1_32718423	32718423	A	1.24E-17	2.40 (1.96-2.93)	0.108	1.23 (0.96-1.59)
4	rs9273012	32719619	G	1.24E-17	2.40 (1.96-2.93)	0.108	1.23 (0.96-1.59)
5	rs2071550	32838918	T	1.55E-17	2.31 (1.91-2.81)	0.0007178	1.47 (1.18-1.84)
6	rs9368741	32845485	A	1.55E-17	2.31 (1.91-2.81)	0.0007178	1.47 (1.18-1.84)
7	rs642093	32690053	A	1.76E-17	2.39 (1.96-2.92)	0.3952	1.12 (0.86-1.47)
8	rs7756741	32691176	A	1.76E-17	2.39 (1.96-2.92)	0.3952	1.12 (0.86-1.47)
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10	AA_DRB1_37_32660037_YL	32660037	P	1.90E-17	2.38 (1.95-2.91)	0.01236	1.36 (1.07-1.73)
11	AA_DRB1_67_32659947_L	32659947	P	3.51E-17	0.35 (0.27-0.45)	6.12E-08	0.48 (0.37-0.63)
12	SNP_DRB1_32659948_G	32659948	P	3.51E-17	0.35 (0.27-0.45)	6.12E-08	0.48 (0.37-0.63)
13	rs7745656	32788948	G	3.89E-17	0.42 (0.34-0.51)	0.0009881	0.68 (0.53-0.85)
14	rs2647087	32789027	A	3.89E-17	0.42 (0.34-0.51)	0.0009881	0.68 (0.53-0.85)
15	rs2647089	32789546	T	3.89E-17	0.42 (0.34-0.51)	0.0009881	0.68 (0.53-0.85)
16	rs6935723	32789647	T	3.89E-17	0.42 (0.34-0.51)	0.0009881	0.68 (0.53-0.85)
17	rs3104404	32790152	C	5.05E-17	0.43 (0.35-0.52)	0.001604	0.69 (0.55-0.87)
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19	AA_DQB1_75_32740612	32740612	V	6.65E-17	0.39 (0.32-0.49)	3.87E-06	0.57 (0.45-0.72)
20	SNP_DQB1_32740613	32740613	C	6.65E-17	0.39 (0.32-0.49)	3.87E-06	0.57 (0.45-0.72)
21	AA_DQB1_74_32740615_E	32740615	A	6.65E-17	0.39 (0.32-0.49)	3.87E-06	0.57 (0.45-0.72)
22	SNP_DQB1_32740615	32740615	G	6.65E-17	0.39 (0.32-0.49)	3.87E-06	0.57 (0.45-0.72)
23	AA_DQB1_71_32740624_T	32740624	A	6.65E-17	0.39 (0.32-0.49)	3.87E-06	0.57 (0.45-0.72)
24	AA_DRB1_32_32660052	32660052	H	1.19E-16	0.33 (0.25-0.43)	2.58E-07	0.48 (0.36-0.63)
25	SNP_DRB1_32660053	32660053	G	1.19E-16	0.33 (0.25-0.43)	2.58E-07	0.48 (0.36-0.63)
26	AA_DQB1_77_32740606	32740606	R	1.19E-16	0.39 (0.31-0.49)	1.36E-06	0.55 (0.43-0.70)
27	SNP_DQB1_32740606	32740606	C	1.19E-16	0.39 (0.31-0.49)	1.36E-06	0.55 (0.43-0.70)
28	AA_DQB1_71_32740624_KA	32740624	P	1.57E-16	0.39 (0.31-0.49)	1.60E-06	0.55 (0.43-0.70)
29	rs2647050	32777745	T	2.18E-16	0.42 (0.34-0.52)	0.001123	0.68 (0.53-0.86)
30	rs2856726	32774699	T	2.41E-16	0.42 (0.34-0.52)	0.001197	0.68 (0.53-0.86)
31	HLA_DQA1_05	32716284	P	2.47E-16	2.30 (1.88-2.80)	0.536	1.09 (0.83-1.42)
32	HLA_DQA1_0501	32716284	P	2.47E-16	2.30 (1.88-2.80)	0.536	1.09 (0.83-1.42)
33	SNP_DQA1_32717075	32717075	C	2.47E-16	2.30 (1.88-2.80)	0.536	1.09 (0.83-1.42)
34	SNP_DQA1_32717255	32717255	C	2.47E-16	2.30 (1.88-2.80)	0.536	1.09 (0.83-1.42)
35	AA_DQA1_75_32717275	32717275	S	2.47E-16	2.30 (1.88-2.80)	0.536	1.09 (0.83-1.42)
36	SNP_DQA1_32717275	32717275	G	2.47E-16	2.30 (1.88-2.80)	0.536	1.09 (0.83-1.42)
37	SNP_DQA1_32717276	32717276	T	2.47E-16	2.30 (1.88-2.80)	0.536	1.09 (0.83-1.42)
38	AA_DQA1_107_32717784_T	32717784	A	2.47E-16	2.30 (1.88-2.80)	0.536	1.09 (0.83-1.42)
39	AA_DQA1_107_32717784_I	32717784	P	2.47E-16	2.30 (1.88-2.80)	0.536	1.09 (0.83-1.42)
40	SNP_DQA1_32717784	32717784	T	2.47E-16	2.30 (1.88-2.80)	0.536	1.09 (0.83-1.42)
41	SNP_DQA1_32717930	32717930	C	2.47E-16	2.30 (1.88-2.80)	0.536	1.09 (0.83-1.42)
42	AA_DQA1_156_32717931_F	32717931	A	2.47E-16	2.30 (1.88-2.80)	0.536	1.09 (0.83-1.42)
43	AA_DQA1_156_32717931_L	32717931	P	2.47E-16	2.30 (1.88-2.80)	0.536	1.09 (0.83-1.42)
44	AA_DQA1_161_32717946_D	32717946	A	2.47E-16	2.30 (1.88-2.80)	0.536	1.09 (0.83-1.42)
45	AA_DQA1_161_32717946_E	32717946	P	2.47E-16	2.30 (1.88-2.80)	0.536	1.09 (0.83-1.42)
46	SNP_DQA1_32717947	32717947	G	2.47E-16	2.30 (1.88-2.80)	0.536	1.09 (0.83-1.42)
47	AA_DQA1_163_32717952_I	32717952	A	2.47E-16	2.30 (1.88-2.80)	0.536	1.09 (0.83-1.42)
48	AA_DQA1_163_32717952_S	32717952	P	2.47E-16	2.30 (1.88-2.80)	0.536	1.09 (0.83-1.42)
49	SNP_DQA1_32717952	32717952	G	2.47E-16	2.30 (1.88-2.80)	0.536	1.09 (0.83-1.42)
50	SNP_DQA1_32717987_A	32717987	P	2.47E-16	2.30 (1.88-2.80)	0.536	1.09 (0.83-1.42)
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AA_DQA1_175_32717988_K	32717988	P	2.47E-16	2.30 (1.88-2.80)	0.536	1.09 (0.83-1.42)
AA_DQA1_175_32717988_QE	32717988	A	2.47E-16	2.30 (1.88-2.80)	0.536	1.09 (0.83-1.42)
rs9368737	32766407	T	4.52E-16	0.42 (0.34-0.52)	0.000948	0.67 (0.53-0.85)
SNP_DRB1_32660045	32660045	C	5.58E-16	0.45 (0.37-0.54)	0.01577	0.75 (0.60-0.95)
rs9275601	32790642	C	5.89E-16	0.45 (0.37-0.54)	0.01008	0.74 (0.59-0.93)
rs9501255	33163076	T	8.20E-16	5.17 (3.47-7.72)	1.95E-19	7.42 (4.80-11.47)
rs7763822	33168406	T	8.20E-16	5.17 (3.47-7.72)	1.95E-19	7.42 (4.80-11.47)
rs7764491	33168818	G	8.20E-16	5.17 (3.47-7.72)	1.95E-19	7.42 (4.80-11.47)
AA_DPB1_35_33156517_Y	33156517	P	1.32E-15	4.13 (2.92-5.85)	7.49E-19	5.77 (3.92-8.49)
SNP_DPB1_33156517	33156517	A	1.32E-15	4.13 (2.92-5.85)	7.49E-19	5.77 (3.92-8.49)
rs9689804	33169170	A	1.55E-15	5.04 (3.39-7.50)	3.28E-19	7.24 (4.70-11.17)
AA_DQB1_57_32740666_D	32740666	A	4.82E-15	0.44 (0.36-0.54)	0.0001688	0.64 (0.51-0.81)
SNP_DQB1_32740666_T	32740666	A	4.82E-15	0.44 (0.36-0.54)	0.0001688	0.64 (0.51-0.81)
rs9296042	32843983	C	5.83E-15	0.46 (0.38-0.56)	0.000623	0.68 (0.54-0.85)
rs2227127	32819760	T	7.65E-15	0.46 (0.38-0.56)	0.0005317	0.68 (0.55-0.85)
AA_DRB1_37_32660037_NF	32660037	P	8.58E-15	0.39 (0.31-0.50)	2.76E-05	0.58 (0.45-0.75)
AA_DRB1_37_32660037_SY	32660037	A	1.04E-14	0.40 (0.32-0.51)	7.15E-05	0.60 (0.47-0.77)
AA_DQB1_67_32740636	32740636	I	1.07E-14	0.36 (0.27-0.46)	3.21E-06	0.51 (0.39-0.68)
SNP_DQB1_32740637	32740637	T	1.07E-14	0.36 (0.27-0.46)	3.21E-06	0.51 (0.39-0.68)
SNP_DQB1_32740638	32740638	G	1.07E-14	0.36 (0.27-0.46)	3.21E-06	0.51 (0.39-0.68)
AA_DQB1_66_32740639	32740639	D	1.07E-14	0.36 (0.27-0.46)	3.21E-06	0.51 (0.39-0.68)
AA_DQB1_57_32740666_AV	32740666	P	1.09E-14	0.43 (0.35-0.53)	1.73E-05	0.60 (0.47-0.75)
SNP_DQB1_32740666_GA	32740666	P	1.09E-14	0.43 (0.35-0.53)	1.73E-05	0.60 (0.47-0.75)
rs9461799	32797507	T	1.13E-14	0.46 (0.38-0.56)	0.0006685	0.68 (0.55-0.85)
rs2858892	32801220	T	1.13E-14	0.46 (0.38-0.56)	0.0006685	0.68 (0.55-0.85)
rs2859112	32805991	G	1.13E-14	0.46 (0.38-0.56)	0.0006685	0.68 (0.55-0.85)
AA_DQB1_37_32740726_Y	32740726	A	1.24E-14	0.34 (0.25-0.44)	7.25E-07	0.47 (0.35-0.64)
SNP_DQB1_32740727_A	32740727	A	1.24E-14	0.34 (0.25-0.44)	7.25E-07	0.47 (0.35-0.64)
rs7744001	32734064	G	1.43E-14	0.46 (0.37-0.56)	0.03502	0.78 (0.61-0.98)
rs9275141	32759095	T	1.68E-14	0.41 (0.33-0.52)	0.0001348	0.62 (0.48-0.79)
rs4642516	32765521	G	1.68E-14	0.41 (0.33-0.52)	0.0001348	0.62 (0.48-0.79)
rs6457644	32814106	C	1.94E-14	0.47 (0.39-0.57)	0.0008172	0.69 (0.55-0.86)
rs3104407	32790430	G	2.59E-14	0.43 (0.35-0.54)	0.0007396	0.66 (0.52-0.84)
rs2859100	32807457	C	5.14E-14	0.47 (0.39-0.58)	0.001149	0.70 (0.56-0.87)
rs482044	32684042	G	5.66E-14	0.43 (0.34-0.54)	0.0004282	0.65 (0.51-0.82)
rs3134930	32299598	A	7.09E-14	2.09 (1.72-2.53)	0.4313	1.10 (0.87-1.40)
rs2858312	32775208	C	1.05E-13	0.47 (0.38-0.57)	0.03917	0.78 (0.62-0.99)
rs2858331	32789255	T	1.50E-13	0.46 (0.38-0.57)	0.005022	0.72 (0.57-0.91)
SNP_DQA1_32717190_C	32717190	A	2.35E-13	2.06 (1.70-2.50)	0.1931	1.17 (0.92-1.48)
AA_DQA1_47_32717191_RQ	32717191	A	2.35E-13	2.06 (1.70-2.50)	0.1931	1.17 (0.92-1.48)
SNP_DQA1_32717217_x	32717217	P	2.35E-13	2.06 (1.70-2.50)	0.1931	1.17 (0.92-1.48)
AA_DQA1_56_32717218_x	32717218	P	2.35E-13	2.06 (1.70-2.50)	0.1931	1.17 (0.92-1.48)
SNP_DQA1_32717219_x	32717219	P	2.35E-13	2.06 (1.70-2.50)	0.1931	1.17 (0.92-1.48)
SNP_DQA1_32717277_C	32717277	P	2.35E-13	2.06 (1.70-2.50)	0.1931	1.17 (0.92-1.48)
AA_DQA1_76_32717278_L	32717278	P	2.35E-13	2.06 (1.70-2.50)	0.1931	1.17 (0.92-1.48)
rs9269081	32549078	C	3.59E-13	0.47 (0.39-0.58)	0.2128	0.86 (0.67-1.09)

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3	rs436845	32305714	C	5.64E-13	1.99 (1.65-2.40)	0.005025	1.35 (1.10-1.67)
4	SNP_DQB1_32737867	32737867	A	6.79E-13	0.45 (0.37-0.56)	0.00244	0.69 (0.54-0.88)
5	rs12182351	32309685	C	7.16E-13	1.99 (1.65-2.41)	0.004956	1.36 (1.10-1.68)
6	rs3130299	32311515	G	7.16E-13	1.99 (1.65-2.41)	0.004956	1.36 (1.10-1.68)
7	rs9469220	32766288	G	7.52E-13	0.46 (0.37-0.56)	0.002626	0.69 (0.55-0.88)
8	rs17208888	32487484	A	7.52E-13	2.07 (1.70-2.53)	0.1161	1.21 (0.95-1.53)
9	AA_DQB1_-10_32742295_A	32742295	A	8.46E-13	0.31 (0.23-0.43)	3.53E-07	0.42 (0.30-0.58)
10	rs378088	32304291	A	1.06E-12	1.98 (1.64-2.39)	0.005995	1.35 (1.09-1.66)
11	rs17577980	32467799	A	1.15E-12	2.06 (1.69-2.51)	0.1251	1.20 (0.95-1.52)
12	SNP_DQB1_32742309_CG	32742309	P	1.21E-12	0.49 (0.40-0.59)	0.03607	0.78 (0.62-0.98)
13	rs9469246	32800205	T	1.27E-12	0.48 (0.39-0.59)	0.0003889	0.67 (0.53-0.83)
14	rs2280774	32036670	T	1.33E-12	1.98 (1.64-2.39)	0.006609	1.34 (1.09-1.66)
15	rs2071286	32287874	A	1.33E-12	2.02 (1.66-2.45)	0.05887	1.24 (0.99-1.56)
16	AA_DRB1_74_32659926_AL	32659926	A	1.97E-12	0.39 (0.30-0.51)	3.63E-05	0.55 (0.42-0.73)
17	SNP_DRB1_32659926_CT	32659926	P	1.97E-12	0.39 (0.30-0.51)	3.63E-05	0.55 (0.42-0.73)
18	rs1800624	32260365	A	2.14E-12	2.01 (1.65-2.44)	0.03934	1.27 (1.01-1.59)
19	rs1035798	32259200	T	2.31E-12	2.00 (1.65-2.43)	0.04445	1.26 (1.01-1.58)
20	SNP_DQB1_32737837	32737837	A	2.52E-12	0.42 (0.33-0.54)	0.0001781	0.61 (0.47-0.79)
21	rs2856717	32778286	T	2.87E-12	0.41 (0.32-0.53)	0.0002978	0.61 (0.47-0.80)
22	SNP_DQB1_32740731	32740731	T	3.26E-12	0.28 (0.20-0.40)	2.21E-07	0.37 (0.25-0.54)
23	rs2858324	32768353	T	3.50E-12	0.41 (0.32-0.53)	0.0003313	0.61 (0.47-0.80)
24	rs2647012	32772436	A	3.50E-12	0.41 (0.32-0.53)	0.0003313	0.61 (0.47-0.80)
25	rs365053	32303966	C	4.01E-12	1.93 (1.61-2.33)	0.008714	1.33 (1.07-1.64)
26	SNP_DQB1_32737205	32737205	T	4.43E-12	0.28 (0.20-0.40)	2.68E-07	0.37 (0.25-0.54)
27	HLA_DQB1_02	32739039	P	4.43E-12	0.28 (0.20-0.40)	2.68E-07	0.37 (0.25-0.54)
28	AA_DQB1_74_32740615_A	32740615	P	4.43E-12	0.28 (0.20-0.40)	2.68E-07	0.37 (0.25-0.54)
29	SNP_DQB1_32740623	32740623	T	4.43E-12	0.28 (0.20-0.40)	2.68E-07	0.37 (0.25-0.54)
30	AA_DQB1_71_32740624_K	32740624	P	4.43E-12	0.28 (0.20-0.40)	2.68E-07	0.37 (0.25-0.54)
31	AA_DQB1_55_32740672_L	32740672	P	4.43E-12	0.28 (0.20-0.40)	2.68E-07	0.37 (0.25-0.54)
32	SNP_DQB1_32740672_A	32740672	P	4.43E-12	0.28 (0.20-0.40)	2.68E-07	0.37 (0.25-0.54)
33	AA_DQB1_52_32740681	32740681	L	4.43E-12	0.28 (0.20-0.40)	2.68E-07	0.37 (0.25-0.54)
34	SNP_DQB1_32740681	32740681	A	4.43E-12	0.28 (0.20-0.40)	2.68E-07	0.37 (0.25-0.54)
35	AA_DQB1_47_32740696	32740696	F	4.43E-12	0.28 (0.20-0.40)	2.68E-07	0.37 (0.25-0.54)
36	SNP_DQB1_32740696	32740696	A	4.43E-12	0.28 (0.20-0.40)	2.68E-07	0.37 (0.25-0.54)
37	AA_DQB1_46_32740699	32740699	E	4.43E-12	0.28 (0.20-0.40)	2.68E-07	0.37 (0.25-0.54)
38	SNP_DQB1_32740699	32740699	T	4.43E-12	0.28 (0.20-0.40)	2.68E-07	0.37 (0.25-0.54)
39	AA_DQB1_37_32740726_I	32740726	P	4.43E-12	0.28 (0.20-0.40)	2.68E-07	0.37 (0.25-0.54)
40	SNP_DQB1_32740726	32740726	A	4.43E-12	0.28 (0.20-0.40)	2.68E-07	0.37 (0.25-0.54)
41	SNP_DQB1_32740727_T	32740727	P	4.43E-12	0.28 (0.20-0.40)	2.68E-07	0.37 (0.25-0.54)
42	AA_DQB1_30_32740747_S	32740747	P	4.43E-12	0.28 (0.20-0.40)	2.68E-07	0.37 (0.25-0.54)
43	SNP_DQB1_32740747	32740747	C	4.43E-12	0.28 (0.20-0.40)	2.68E-07	0.37 (0.25-0.54)
44	SNP_DQB1_32740748_T	32740748	P	4.43E-12	0.28 (0.20-0.40)	2.68E-07	0.37 (0.25-0.54)
45	AA_DQB1_28_32740753	32740753	S	4.43E-12	0.28 (0.20-0.40)	2.68E-07	0.37 (0.25-0.54)
46	SNP_DQB1_32740753	32740753	C	4.43E-12	0.28 (0.20-0.40)	2.68E-07	0.37 (0.25-0.54)
47	SNP_DQB1_32740773_T	32740773	P	4.43E-12	0.28 (0.20-0.40)	2.68E-07	0.37 (0.25-0.54)
48	AA_DQB1_-10_32742295_S	32742295	P	4.43E-12	0.28 (0.20-0.40)	2.68E-07	0.37 (0.25-0.54)
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SNP_DQB1_32742296_A	32742296	P	4.43E-12	0.28 (0.20-0.40)	2.68E-07	0.37 (0.25-0.54)
rs3891175	32742445	A	4.43E-12	0.28 (0.20-0.40)	2.68E-07	0.37 (0.25-0.54)
rs6941112	32054593	A	4.69E-12	1.96 (1.62-2.37)	0.00872	1.33 (1.08-1.65)
rs9275516	32782621	A	5.16E-12	0.43 (0.34-0.55)	0.001042	0.65 (0.50-0.84)
rs6932517	32786160	C	5.16E-12	0.43 (0.34-0.55)	0.001042	0.65 (0.50-0.84)
AA_DQB1_71_32740624_KD	32740624	P	5.23E-12	0.33 (0.24-0.45)	2.25E-06	0.44 (0.32-0.62)
SNP_DQB1_32740624	32740624	T	5.23E-12	0.33 (0.24-0.45)	2.25E-06	0.44 (0.32-0.62)
AA_DQB1_57_32740666_A	32740666	P	5.31E-12	0.41 (0.32-0.53)	2.08E-05	0.55 (0.42-0.73)
SNP_DQB1_32740666_G	32740666	P	5.31E-12	0.41 (0.32-0.53)	2.08E-05	0.55 (0.42-0.73)
rs2858332	32789139	C	6.56E-12	0.45 (0.36-0.57)	0.001829	0.68 (0.53-0.86)
SNP_DQB1_32740773_C	32740773	A	7.29E-12	0.33 (0.24-0.45)	2.74E-06	0.45 (0.32-0.62)
rs17500468	32819156	G	8.24E-12	2.10 (1.69-2.59)	0.2844	1.15 (0.89-1.48)
AA_DRB1_74_32659926_RE	32659926	P	8.87E-12	0.31 (0.22-0.43)	3.27E-06	0.43 (0.30-0.61)
rs495089	32305441	C	1.17E-11	0.47 (0.37-0.58)	0.0005024	0.65 (0.52-0.83)
rs2228628	32196832	G	1.34E-11	1.95 (1.60-2.36)	0.01448	1.31 (1.06-1.63)
AA_DQB1_57_32740666_AS	32740666	P	1.44E-11	0.46 (0.37-0.58)	0.0005106	0.65 (0.50-0.83)
SNP_DQB1_32740666_GC	32740666	P	1.44E-11	0.46 (0.37-0.58)	0.0005106	0.65 (0.50-0.83)
rs6902493	32130876	T	1.68E-11	1.93 (1.60-2.34)	0.02247	1.29 (1.04-1.60)
rs7774434	32765556	C	1.79E-11	0.49 (0.40-0.61)	0.02189	0.76 (0.60-0.96)
rs2857009	32127724	G	2.01E-11	1.93 (1.59-2.34)	0.0253	1.28 (1.03-1.59)
rs6923504	32536164	C	2.21E-11	0.51 (0.42-0.62)	0.2795	0.88 (0.69-1.11)
rs6903608	32536263	T	2.21E-11	0.51 (0.42-0.62)	0.2795	0.88 (0.69-1.11)
rs2239689	32138262	T	2.43E-11	1.92 (1.59-2.33)	0.02498	1.28 (1.03-1.59)
rs9269110	32551247	C	2.44E-11	0.51 (0.42-0.62)	0.3008	0.88 (0.70-1.12)
AA_DQB1_26_32740759_L	32740759	P	2.65E-11	0.50 (0.40-0.61)	0.01936	0.76 (0.60-0.96)
SNP_DQB1_32740759_A	32740759	P	2.65E-11	0.50 (0.40-0.61)	0.01936	0.76 (0.60-0.96)
SNP_DQB1_32740760_G	32740760	P	2.65E-11	0.50 (0.40-0.61)	0.01936	0.76 (0.60-0.96)
rs11244	32888701	T	3.10E-11	1.92 (1.59-2.33)	0.07261	1.23 (0.98-1.53)
rs2071295	32146678	A	3.12E-11	1.92 (1.58-2.32)	0.03092	1.27 (1.02-1.58)
AA_DQA1_47_32717191_RK	32717191	P	3.33E-11	0.52 (0.42-0.63)	0.4149	0.91 (0.72-1.15)
AA_DQA1_52_32717206_R	32717206	A	3.33E-11	0.52 (0.42-0.63)	0.4149	0.91 (0.72-1.15)
rs7766862	32140985	A	3.39E-11	1.91 (1.58-2.32)	0.02713	1.28 (1.03-1.59)
rs9271588	32698931	C	3.45E-11	0.49 (0.39-0.60)	0.008162	0.73 (0.57-0.92)
rs9268882	32539601	C	3.70E-11	0.51 (0.42-0.62)	0.3293	0.89 (0.70-1.13)
AA_DRB1_47_32660007	32660007	Y	4.01E-11	0.50 (0.41-0.62)	0.05445	0.80 (0.63-1.00)
SNP_DRB1_32660007	32660007	T	4.01E-11	0.50 (0.41-0.62)	0.05445	0.80 (0.63-1.00)
AA_DRB1_74_32659926_A	32659926	A	5.57E-11	0.44 (0.35-0.57)	0.001107	0.65 (0.50-0.84)
SNP_DRB1_32659926_G	32659926	A	5.57E-11	0.44 (0.35-0.57)	0.001107	0.65 (0.50-0.84)
rs2072632	32029454	T	6.12E-11	1.86 (1.55-2.24)	0.002182	1.38 (1.12-1.69)
AA_DRB1_13_32660109_S	32660109	P	6.37E-11	1.95 (1.60-2.39)	0.987	1.00 (0.78-1.28)
SNP_DRB1_32660109_G	32660109	P	6.37E-11	1.95 (1.60-2.39)	0.987	1.00 (0.78-1.28)
rs9275698	32795951	G	8.96E-11	0.50 (0.40-0.61)	0.001999	0.70 (0.55-0.88)
rs4713505	32212979	T	8.97E-11	1.88 (1.55-2.27)	0.03103	1.27 (1.02-1.58)
rs3129882	32517508	A	9.96E-11	0.51 (0.42-0.63)	0.02126	0.76 (0.61-0.96)
AA_DRB1_26_32660070_F	32660070	A	1.09E-10	0.38 (0.28-0.51)	1.85E-05	0.50 (0.36-0.69)
rs9391753	33206837	G	1.41E-10	1.91 (1.57-2.33)	2.28E-06	1.68 (1.36-2.09)

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3	rs9267803	32209740	T	1.69E-10	1.87 (1.54-2.26)	0.06058	1.23 (0.99-1.53)
4	rs2844458	31959448	T	1.77E-10	1.83 (1.52-2.20)	0.00274	1.37 (1.11-1.68)
5	rs8111	32191153	A	1.77E-10	1.86 (1.54-2.26)	0.0492	1.24 (1.00-1.55)
6	rs6936863	32792007	G	2.40E-10	0.48 (0.39-0.61)	0.002602	0.69 (0.54-0.88)
7	rs5024431	32792322	A	2.40E-10	0.48 (0.39-0.61)	0.002602	0.69 (0.54-0.88)
8	rs1800454	32908390	A	2.57E-10	2.10 (1.67-2.64)	0.9968	1.00 (0.75-1.33)
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10	AA_DRB1_37_32660037_N	32660037	P	2.82E-10	0.37 (0.27-0.51)	0.000105	0.53 (0.38-0.73)
11	SNP_DRB1_32660038_T	32660038	P	2.82E-10	0.37 (0.27-0.51)	0.000105	0.53 (0.38-0.73)
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13	AA_DRB1_37_32660037_YF	32660037	A	2.94E-10	0.53 (0.43-0.64)	0.2026	0.86 (0.68-1.08)
14	rs7750000	33211299	A	3.10E-10	1.89 (1.55-2.30)	4.91E-06	1.66 (1.33-2.06)
15	AA_DRB1_37_32660037_NL	32660037	P	3.18E-10	0.39 (0.29-0.52)	0.0003319	0.57 (0.41-0.77)
16	SNP_DRB1_32660038_A	32660038	A	3.18E-10	0.39 (0.29-0.52)	0.0003319	0.57 (0.41-0.77)
17	rs2736428	31951903	A	3.61E-10	1.81 (1.50-2.17)	0.004732	1.34 (1.09-1.65)
18	rs9268541	32492505	C	3.69E-10	0.30 (0.21-0.44)	3.96E-06	0.39 (0.26-0.58)
19	rs9276612	32850690	A	3.96E-10	1.84 (1.52-2.22)	0.1253	1.19 (0.95-1.48)
20	rs9276644	32853021	C	3.96E-10	1.84 (1.52-2.22)	0.1253	1.19 (0.95-1.48)
21	rs9267810	32229572	C	4.07E-10	1.82 (1.51-2.20)	0.1695	1.17 (0.94-1.45)
22	rs2269424	32240211	T	4.07E-10	1.82 (1.51-2.20)	0.1695	1.17 (0.94-1.45)
23	rs9267817	32247791	A	4.07E-10	1.82 (1.51-2.20)	0.1695	1.17 (0.94-1.45)
24	rs2763982	31980530	G	4.09E-10	0.55 (0.46-0.67)	0.002143	0.73 (0.59-0.89)
25	rs1480383	32848834	G	4.09E-10	1.84 (1.52-2.23)	0.1277	1.19 (0.95-1.48)
26	rs2071293	32170665	T	4.46E-10	1.83 (1.51-2.21)	0.09653	1.20 (0.97-1.49)
27							
28	AA_DPB1_35_33156517_F	33156517	A	4.55E-10	2.57 (1.91-3.47)	4.62E-14	3.61 (2.58-5.03)
29	AA_DRB1_37_32660037_NS	32660037	P	5.45E-10	0.53 (0.43-0.65)	0.1543	0.85 (0.67-1.07)
30	AA_DRB1_71_32659935_K	32659935	P	5.92E-10	0.27 (0.18-0.41)	1.08E-05	0.38 (0.25-0.59)
31	rs17421624	32174155	C	5.92E-10	1.82 (1.51-2.21)	0.1036	1.20 (0.96-1.49)
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33	AA_DRB1_74_32659926_AQ	32659926	A	6.61E-10	0.39 (0.29-0.53)	0.0003757	0.56 (0.41-0.77)
34	AA_DRB1_233_32656004_R	32656004	A	6.75E-10	0.53 (0.44-0.65)	0.9686	1.01 (0.79-1.28)
35	SNP_DQA1_32717151	32717151	G	8.11E-10	0.51 (0.41-0.63)	0.0234	0.76 (0.60-0.96)
36	AA_DQA1_34_32717152	32717152	E	8.11E-10	0.51 (0.41-0.63)	0.0234	0.76 (0.60-0.96)
37	rs707939	31834667	G	8.81E-10	0.56 (0.46-0.67)	0.02981	0.79 (0.64-0.98)
38	rs4394270	32817942	C	9.85E-10	0.48 (0.38-0.61)	0.0002718	0.63 (0.49-0.81)
39	SNP_DQB1_32742309_C	32742309	P	9.97E-10	0.49 (0.39-0.61)	0.005889	0.70 (0.55-0.90)
40	SNP_DRB1_32656004	32656004	G	1.01E-09	0.54 (0.44-0.66)	0.9131	1.01 (0.79-1.29)
41	rs2075800	31885925	A	1.39E-09	1.76 (1.47-2.11)	0.01043	1.30 (1.06-1.60)
42	rs9469378	33267642	C	1.52E-09	2.69 (1.95-3.70)	7.39E-10	3.01 (2.12-4.27)
43	AA_DRB1_26_32660070_Y	32660070	P	1.66E-09	0.19 (0.11-0.32)	1.28E-06	0.25 (0.14-0.43)
44	SNP_DRB1_32660070	32660070	T	1.66E-09	0.19 (0.11-0.32)	1.28E-06	0.25 (0.14-0.43)
45	rs1612904	32776996	G	1.93E-09	0.44 (0.34-0.58)	0.001867	0.63 (0.48-0.85)
46	rs2050190	32447054	C	2.17E-09	1.76 (1.47-2.12)	0.0138	1.30 (1.05-1.59)
47	AA_DRB1_13_32660109_SG	32660109	A	2.31E-09	0.54 (0.44-0.66)	0.7426	0.96 (0.76-1.22)
48	AA_DRB1_12_32660112	32660112	K	2.31E-09	0.54 (0.44-0.66)	0.7426	0.96 (0.76-1.22)
49	SNP_DRB1_32660112	32660112	T	2.31E-09	0.54 (0.44-0.66)	0.7426	0.96 (0.76-1.22)
50	AA_DRB1_11_32660115_S	32660115	A	2.31E-09	0.54 (0.44-0.66)	0.7426	0.96 (0.76-1.22)
51	SNP_DRB1_32660116_A	32660116	A	2.31E-09	0.54 (0.44-0.66)	0.7426	0.96 (0.76-1.22)
52	SNP_DRB1_32660117	32660117	C	2.31E-09	0.54 (0.44-0.66)	0.7426	0.96 (0.76-1.22)
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AA_DRB1_10_32660118_Y	32660118	A	2.31E-09	0.54 (0.44-0.66)	0.7426	0.96 (0.76-1.22)
SNP_DRB1_32660119_A	32660119	A	2.31E-09	0.54 (0.44-0.66)	0.7426	0.96 (0.76-1.22)
SNP_DQB1_32742319_G	32742319	P	2.51E-09	1.79 (1.48-2.17)	0.4883	0.92 (0.72-1.17)
SNP_DQB1_32742351_T	32742351	P	2.51E-09	1.79 (1.48-2.17)	0.4883	0.92 (0.72-1.17)
rs169494	32205854	T	2.59E-09	0.43 (0.33-0.57)	5.75E-05	0.54 (0.40-0.73)
AA_DRB1_70_32659938_Q	32659938	P	2.92E-09	0.52 (0.42-0.65)	0.09633	0.81 (0.64-1.04)
rs2858867	32683303	T	3.15E-09	0.56 (0.46-0.68)	0.8951	1.02 (0.80-1.29)
SNP_DRB1_32657430	32657430	C	3.18E-09	0.54 (0.44-0.67)	0.7792	0.97 (0.76-1.23)
AA_DRB1_149_32657431_H	32657431	A	3.18E-09	0.54 (0.44-0.67)	0.7792	0.97 (0.76-1.23)
AA_DRB1_149_32657431_Q	32657431	P	3.18E-09	0.54 (0.44-0.67)	0.7792	0.97 (0.76-1.23)
SNP_DRB1_32657475	32657475	G	3.18E-09	0.54 (0.44-0.67)	0.7792	0.97 (0.76-1.23)
SNP_DQB1_32742281_G	32742281	A	3.20E-09	0.54 (0.44-0.66)	0.1322	0.84 (0.67-1.06)
SNP_DQB1_32742291_C	32742291	A	3.20E-09	0.54 (0.44-0.66)	0.1322	0.84 (0.67-1.06)
SNP_DQB1_32742347_C	32742347	A	3.20E-09	0.54 (0.44-0.66)	0.1322	0.84 (0.67-1.06)
AA_DRB1_11_32660115_SL	32660115	A	3.47E-09	0.54 (0.44-0.66)	0.4596	0.91 (0.72-1.16)
rs411337	32185358	A	3.47E-09	0.44 (0.33-0.57)	4.59E-05	0.54 (0.40-0.73)
rs9275596	32789609	C	3.64E-09	0.45 (0.34-0.58)	0.002682	0.65 (0.48-0.86)
rs6936428	32847152	T	3.74E-09	0.55 (0.46-0.67)	0.04363	0.80 (0.64-0.99)
AA_DRB1_233_32656004_T	32656004	P	4.08E-09	0.55 (0.45-0.67)	0.93	0.99 (0.78-1.26)
rs2269426	32184477	T	4.33E-09	1.76 (1.46-2.13)	0.01604	1.30 (1.05-1.60)
AA_DRB1_71_32659935_R	32659935	A	4.62E-09	0.55 (0.45-0.67)	0.6858	0.95 (0.76-1.20)
SNP_DRB1_32659935_C	32659935	A	4.62E-09	0.55 (0.45-0.67)	0.6858	0.95 (0.76-1.20)
AA_DQB1_220_32737119_H	32737119	A	5.63E-09	0.56 (0.46-0.68)	0.3693	0.90 (0.72-1.13)
rs8283	32191278	C	6.13E-09	0.51 (0.41-0.64)	0.00116	0.67 (0.52-0.85)
rs17429444	32894046	G	6.17E-09	1.82 (1.49-2.23)	0.4595	1.09 (0.86-1.39)
SNP_DQB1_32742284_T	32742284	A	6.55E-09	0.56 (0.46-0.68)	0.3835	0.90 (0.72-1.14)
rs430916	32296077	T	7.33E-09	1.73 (1.44-2.08)	0.3142	1.12 (0.90-1.38)
rs9267845	32301676	T	7.68E-09	0.58 (0.48-0.70)	0.04842	0.81 (0.66-1.00)
rs1475961	32302587	C	7.68E-09	0.58 (0.48-0.70)	0.04842	0.81 (0.66-1.00)
rs3096691	32302832	A	7.68E-09	0.58 (0.48-0.70)	0.04842	0.81 (0.66-1.00)
rs5021728	32686631	G	7.86E-09	1.76 (1.45-2.13)	0.1904	0.85 (0.66-1.09)
rs502771	32686948	G	7.86E-09	1.76 (1.45-2.13)	0.1904	0.85 (0.66-1.09)
rs707919	31749118	T	8.00E-09	0.58 (0.48-0.70)	0.07459	0.83 (0.67-1.02)
rs415929	32297010	G	8.00E-09	1.70 (1.42-2.04)	0.1415	1.17 (0.95-1.43)
rs9268626	32513022	C	8.05E-09	0.32 (0.21-0.47)	2.41E-05	0.41 (0.27-0.62)
rs2736176	31695540	C	8.10E-09	0.58 (0.48-0.70)	0.07032	0.82 (0.67-1.02)
AA_DQB1_221_32737116_H	32737116	A	8.19E-09	0.56 (0.46-0.68)	0.397	0.91 (0.72-1.14)
AA_DQB1_55_32740672_R	32740672	P	8.48E-09	0.56 (0.46-0.68)	0.5984	0.94 (0.75-1.18)
SNP_DQB1_32740672_C	32740672	P	8.48E-09	0.56 (0.46-0.68)	0.5984	0.94 (0.75-1.18)
SNP_DQB1_32736000	32736000	A	8.50E-09	0.56 (0.46-0.68)	0.4184	0.91 (0.72-1.14)
rs755714	31717792	C	8.89E-09	0.58 (0.48-0.70)	0.07185	0.82 (0.67-1.02)
AA_DQB1_86_32740579_EG	32740579	A	9.19E-09	0.55 (0.45-0.67)	0.2731	0.88 (0.70-1.11)
SNP_DQB1_32740579_G	32740579	P	9.19E-09	0.55 (0.45-0.67)	0.2731	0.88 (0.70-1.11)
rs5026743	32547942	T	9.22E-09	0.55 (0.45-0.68)	0.6755	0.95 (0.75-1.20)
HLA_DQB1_0201	32739039	P	9.55E-09	0.23 (0.14-0.38)	8.06E-06	0.30 (0.18-0.51)
rs805297	31730585	G	9.97E-09	0.58 (0.48-0.70)	0.08137	0.83 (0.67-1.02)

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3	rs423023	32296275	G	1.00E-08	1.70 (1.42-2.03)	0.1763	1.15 (0.94-1.42)
4	AA_DRB1_74_32659926_RQ	32659926	P	1.08E-08	0.40 (0.30-0.55)	0.000444	0.55 (0.40-0.77)
5	AA_DRB1_73_32659929	32659929	G	1.08E-08	0.40 (0.30-0.55)	0.000444	0.55 (0.40-0.77)
6	SNP_DRB1_32659929	32659929	C	1.08E-08	0.40 (0.30-0.55)	0.000444	0.55 (0.40-0.77)
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8	rs9275653	32793843	G	1.13E-08	0.55 (0.44-0.67)	0.02459	0.77 (0.61-0.97)
9	rs7738815	33128365	C	1.14E-08	4.33 (2.62-7.16)	6.72E-11	6.06 (3.53-10.40)
10	rs10807113	32830164	C	1.17E-08	0.54 (0.44-0.67)	0.02972	0.77 (0.61-0.98)
11	rs6918223	32830510	A	1.17E-08	0.54 (0.44-0.67)	0.02972	0.77 (0.61-0.98)
12	rs7770024	32831319	A	1.17E-08	0.54 (0.44-0.67)	0.02972	0.77 (0.61-0.98)
13	rs7769979	32831550	G	1.17E-08	0.54 (0.44-0.67)	0.02972	0.77 (0.61-0.98)
14	rs7774452	32831847	T	1.17E-08	0.54 (0.44-0.67)	0.02972	0.77 (0.61-0.98)
15	rs7756516	32831895	C	1.17E-08	0.54 (0.44-0.67)	0.02972	0.77 (0.61-0.98)
16	rs3213490	32832236	G	1.17E-08	0.54 (0.44-0.67)	0.02972	0.77 (0.61-0.98)
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18	AA_DRB1_11_32660115_SD	32660115	A	1.17E-08	0.56 (0.45-0.68)	0.9366	0.99 (0.78-1.26)
19	rs377763	32307122	T	1.22E-08	0.45 (0.34-0.59)	0.002015	0.63 (0.47-0.84)
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21	SNP_DQB1_32737115	32737115	T	1.25E-08	0.56 (0.46-0.69)	0.4586	0.92 (0.73-1.15)
22	SNP_DQB1_32737119	32737119	C	1.25E-08	0.56 (0.46-0.69)	0.4586	0.92 (0.73-1.15)
23	AA_DQB1_125_32737913_A	32737913	A	1.25E-08	0.56 (0.46-0.69)	0.4586	0.92 (0.73-1.15)
24	SNP_DQB1_32737913	32737913	C	1.25E-08	0.56 (0.46-0.69)	0.4586	0.92 (0.73-1.15)
25	SNP_DQB1_32740556	32740556	T	1.25E-08	0.56 (0.46-0.69)	0.4586	0.92 (0.73-1.15)
26	SNP_DQB1_32740559	32740559	T	1.25E-08	0.56 (0.46-0.69)	0.4586	0.92 (0.73-1.15)
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28	AA_DQB1_90_32740567_T	32740567	A	1.25E-08	0.56 (0.46-0.69)	0.4586	0.92 (0.73-1.15)
29	SNP_DQB1_32740567	32740567	A	1.25E-08	0.56 (0.46-0.69)	0.4586	0.92 (0.73-1.15)
30	AA_DQB1_89_32740570_T	32740570	A	1.25E-08	0.56 (0.46-0.69)	0.4586	0.92 (0.73-1.15)
31	SNP_DQB1_32740570	32740570	C	1.25E-08	0.56 (0.46-0.69)	0.4586	0.92 (0.73-1.15)
32	SNP_DQB1_32740571	32740571	C	1.25E-08	0.56 (0.46-0.69)	0.4586	0.92 (0.73-1.15)
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34	AA_DQB1_87_32740576_L	32740576	A	1.25E-08	0.56 (0.46-0.69)	0.4586	0.92 (0.73-1.15)
35	SNP_DQB1_32740577	32740577	A	1.25E-08	0.56 (0.46-0.69)	0.4586	0.92 (0.73-1.15)
36	AA_DQB1_86_32740579_E	32740579	A	1.25E-08	0.56 (0.46-0.69)	0.4586	0.92 (0.73-1.15)
37	SNP_DQB1_32740579_T	32740579	A	1.25E-08	0.56 (0.46-0.69)	0.4586	0.92 (0.73-1.15)
38	AA_DQB1_85_32740582_L	32740582	A	1.25E-08	0.56 (0.46-0.69)	0.4586	0.92 (0.73-1.15)
39	SNP_DQB1_32740583	32740583	C	1.25E-08	0.56 (0.46-0.69)	0.4586	0.92 (0.73-1.15)
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41	AA_DQB1_84_32740585_Q	32740585	A	1.25E-08	0.56 (0.46-0.69)	0.4586	0.92 (0.73-1.15)
42	SNP_DQB1_32740586	32740586	C	1.25E-08	0.56 (0.46-0.69)	0.4586	0.92 (0.73-1.15)
43	AA_DQB1_53_32740678	32740678	Q	1.25E-08	0.56 (0.46-0.69)	0.4586	0.92 (0.73-1.15)
44	SNP_DQB1_32740678	32740678	T	1.25E-08	0.56 (0.46-0.69)	0.4586	0.92 (0.73-1.15)
45	SNP_DQB1_32742278_C	32742278	A	1.25E-08	0.56 (0.46-0.69)	0.4586	0.92 (0.73-1.15)
46	SNP_DQB1_32742284_TC	32742284	A	1.25E-08	0.56 (0.46-0.69)	0.4586	0.92 (0.73-1.15)
47	SNP_DQB1_32742309_CA	32742309	A	1.25E-08	0.56 (0.46-0.69)	0.4586	0.92 (0.73-1.15)
48	SNP_DQB1_32742328_C	32742328	A	1.25E-08	0.56 (0.46-0.69)	0.4586	0.92 (0.73-1.15)
49	AA_DQB1_86_32740579_A	32740579	P	1.33E-08	0.55 (0.45-0.68)	0.2961	0.88 (0.70-1.11)
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51	rs9268877	32539125	G	1.35E-08	0.55 (0.45-0.68)	0.7194	0.96 (0.76-1.21)
52	rs9273327	32731201	C	1.35E-08	0.18 (0.10-0.33)	4.05E-06	0.24 (0.13-0.44)
53	rs2854275	32736406	T	1.35E-08	0.18 (0.10-0.33)	4.05E-06	0.24 (0.13-0.44)
54	rs3129716	32765414	C	1.35E-08	0.18 (0.10-0.33)	4.05E-06	0.24 (0.13-0.44)
55	rs2856674	32767623	C	1.35E-08	0.18 (0.10-0.33)	4.05E-06	0.24 (0.13-0.44)
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AA_DRB1_71_32659935_KE	32659935	P	1.39E-08	0.51 (0.40-0.64)	0.0568	0.78 (0.60-1.01)
SNP_DRB1_32659935_T	32659935	P	1.39E-08	0.51 (0.40-0.64)	0.0568	0.78 (0.60-1.01)
rs3129302	33082320	A	1.40E-08	3.72 (2.36-5.85)	8.99E-11	4.99 (3.07-8.12)
rs492899	32041497	G	1.45E-08	0.42 (0.31-0.57)	4.10E-05	0.51 (0.37-0.71)
rs1059615	32657541	T	1.48E-08	0.20 (0.11-0.34)	6.40E-06	0.26 (0.14-0.47)
SNP_DRB1_32657541	32657541	A	1.48E-08	0.20 (0.11-0.34)	6.40E-06	0.26 (0.14-0.47)
HLA_DRB1_0301	32660042	P	1.48E-08	0.20 (0.11-0.34)	6.40E-06	0.26 (0.14-0.47)
rs11758312	32824350	C	1.61E-08	0.55 (0.44-0.67)	0.03327	0.78 (0.62-0.98)
rs5016066	32826796	A	1.61E-08	0.55 (0.44-0.67)	0.03327	0.78 (0.62-0.98)
AA_DRB1_11_32660115_SLD	32660115	A	1.68E-08	0.55 (0.45-0.68)	0.6208	0.94 (0.74-1.20)
AA_DQB1_221_32737116_Q	32737116	P	1.80E-08	0.57 (0.46-0.69)	0.4902	0.92 (0.73-1.16)
AA_DQB1_220_32737119_R	32737119	P	1.80E-08	0.57 (0.46-0.69)	0.4902	0.92 (0.73-1.16)
AA_DQB1_125_32737913_Ax	32737913	A	1.80E-08	0.57 (0.46-0.69)	0.4902	0.92 (0.73-1.16)
AA_DQB1_90_32740567_I	32740567	P	1.80E-08	0.57 (0.46-0.69)	0.4902	0.92 (0.73-1.16)
AA_DQB1_89_32740570_G	32740570	P	1.80E-08	0.57 (0.46-0.69)	0.4902	0.92 (0.73-1.16)
AA_DQB1_87_32740576_Lx	32740576	A	1.80E-08	0.57 (0.46-0.69)	0.4902	0.92 (0.73-1.16)
AA_DQB1_86_32740579_Ex	32740579	A	1.80E-08	0.57 (0.46-0.69)	0.4902	0.92 (0.73-1.16)
AA_DQB1_85_32740582_V	32740582	P	1.80E-08	0.57 (0.46-0.69)	0.4902	0.92 (0.73-1.16)
AA_DQB1_84_32740585_E	32740585	P	1.80E-08	0.57 (0.46-0.69)	0.4902	0.92 (0.73-1.16)
rs805262	31736712	G	1.82E-08	0.57 (0.47-0.69)	0.02021	0.77 (0.62-0.96)
rs4713506	32221958	A	1.83E-08	1.71 (1.42-2.06)	0.3548	1.11 (0.89-1.38)
SNP_DQA1_32713252	32713252	T	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
HLA_DQA1_01	32716284	P	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
AA_DQA1_11_32717083_C	32717083	P	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
AA_DQA1_11_32717083_Y	32717083	A	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
SNP_DQA1_32717083	32717083	G	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
AA_DQA1_18_32717104	32717104	F	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
SNP_DQA1_32717104	32717104	T	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
AA_DQA1_45_32717185	32717185	A	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
SNP_DQA1_32717185	32717185	C	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
AA_DQA1_47_32717191_R	32717191	P	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
AA_DQA1_48_32717194	32717194	W	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
SNP_DQA1_32717194	32717194	G	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
AA_DQA1_50_32717200_E	32717200	P	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
SNP_DQA1_32717200	32717200	A	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
AA_DQA1_52_32717206_S	32717206	P	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
AA_DQA1_53_32717209_K	32717209	P	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
SNP_DQA1_32717214	32717214	G	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
AA_DQA1_55_32717215	32717215	G	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
SNP_DQA1_32717217_G	32717217	P	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
AA_DQA1_56_32717218_G	32717218	P	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
SNP_DQA1_32717219_T	32717219	P	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
SNP_DQA1_32717231	32717231	G	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
SNP_DQA1_32717232	32717232	G	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
AA_DQA1_61_32717233	32717233	G	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
SNP_DQA1_32717233	32717233	G	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)

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3	AA_DQA1_64_32717242	32717242	R	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
4	SNP_DQA1_32717242	32717242	G	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
5	AA_DQA1_66_32717248	32717248	M	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
6	SNP_DQA1_32717249	32717249	G	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
7	SNP_DQA1_32717256_G	32717256	P	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
8	AA_DQA1_69_32717257_A	32717257	P	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
9	SNP_DQA1_32717277_A	32717277	P	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
10	AA_DQA1_76_32717278_M	32717278	P	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
11	AA_DQA1_80_32717290	32717290	Y	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
12	SNP_DQA1_32717290	32717290	A	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
13	SNP_DQA1_32717987_C	32717987	P	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
14	AA_DQA1_175_32717988_Q	32717988	P	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
15	AA_DQA1_175_32717988_Qx	32717988	P	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
16	AA_DQA1_218_32718473_Q	32718473	P	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
17	AA_DQA1_218_32718473_R	32718473	A	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
18	SNP_DQA1_32718473	32718473	A	1.88E-08	0.57 (0.47-0.69)	0.52	0.93 (0.74-1.17)
19	AA_DRB1_77_32659917	32659917	N	1.92E-08	0.21 (0.12-0.36)	8.92E-06	0.28 (0.16-0.49)
20	SNP_DRB1_32659917	32659917	T	1.92E-08	0.21 (0.12-0.36)	8.92E-06	0.28 (0.16-0.49)
21	AA_DRB1_74_32659926_R	32659926	P	1.92E-08	0.21 (0.12-0.36)	8.92E-06	0.28 (0.16-0.49)
22	SNP_DRB1_32659926_C	32659926	P	1.92E-08	0.21 (0.12-0.36)	8.92E-06	0.28 (0.16-0.49)
23	HLA_DRB1_03	32660042	P	1.92E-08	0.21 (0.12-0.36)	8.92E-06	0.28 (0.16-0.49)
24	rs2260050	31699907	T	2.04E-08	0.57 (0.47-0.69)	0.02036	0.77 (0.62-0.96)
25	rs404890	32306845	T	2.25E-08	1.69 (1.41-2.03)	0.07042	1.21 (0.98-1.49)
26	AA_DRB1_71_32659935_KA	32659935	P	2.35E-08	0.50 (0.40-0.64)	0.06854	0.78 (0.60-1.02)
27	rs2259571	31691806	A	3.72E-08	0.58 (0.47-0.70)	0.03058	0.79 (0.63-0.98)
28	AA_B_109_31432144_L	31432144	A	4.30E-08	2.60 (1.85-3.66)	0.3747	1.19 (0.81-1.77)
29	AA_DRB1_13_32660109_SY	32660109	A	4.62E-08	0.57 (0.47-0.70)	0.8756	1.02 (0.80-1.29)
30	rs2187668	32713862	A	4.68E-08	0.23 (0.13-0.39)	2.05E-05	0.30 (0.17-0.52)
31	rs2284189	32715374	C	4.68E-08	0.23 (0.13-0.39)	2.05E-05	0.30 (0.17-0.52)
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Supplementary Table S4. HLA classical alleles, SNPs and amino acid variants associated with systemic sclerosis at the genome-wide significance level ($p < 5 \times 10^{-8}$) in the Iranian and the Turkish cohorts. The results of the conditioned analysis are also shown. The marker nomenclature is as follow: 1) Classical HLA alleles: HLA_[gene]_[allele]; 2) HLA amino acids: AA_[gene]_[amino acid position within the molecule]_[genetic position of the center of codon]_[allele]; 3) HLA intragenic SNPs: SNP_[gene]_[genetic position]_[allele]; 4) Insertions/deletions: [variant]_[gene]_[genetic position]_[insertion/x=deletion]. When more than one allele is shown, it refers to the presence of any of them. *For binary encodings, P=present, A=absent.

Variation	Position in Chr 6 (GRCh36)	Allele	Iran				Turkey			
			Unconditioned		Conditioned on HLA-DRB1*11:04		Unconditioned		Conditioned on HLA-DRB1*11:04	
			p value	OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)
HLA_DRB1_1104	32660042	P	2.10E-24	3.14 (2.52-3.91)	NA	NA	4.90E-11	2.93 (2.12-4.03)	NA	NA
HLA_DRB1_11	32660042	P	5.39E-22	2.57 (2.12-3.11)	2.25E-03	1.56 (1.17-2.07)	9.42E-08	2.13 (1.61-2.81)	5.50E-01	1.14 (0.74-1.74)
AA_DRB1_58_32659974_E	32659974	P	5.39E-22	2.57 (2.12-3.11)	2.25E-03	1.56 (1.17-2.07)	1.09E-07	2.12 (1.61-2.80)	5.73E-01	1.13 (0.74-1.73)
SNP_DRB1_32659974_T	32659974	P	5.39E-22	2.57 (2.12-3.11)	2.25E-03	1.56 (1.17-2.07)	1.09E-07	2.12 (1.61-2.80)	5.73E-01	1.13 (0.74-1.73)
AA_DRB1_58_32659974_A	32659974	A	8.70E-22	2.55 (2.11-3.09)	2.84E-03	1.54 (1.16-2.04)	9.42E-08	2.13 (1.61-2.81)	5.50E-01	1.14 (0.74-1.74)
SNP_DRB1_32659974_G	32659974	A	8.70E-22	2.55 (2.11-3.09)	2.84E-03	1.54 (1.16-2.04)	9.42E-08	2.13 (1.61-2.81)	5.50E-01	1.14 (0.74-1.74)
AA_DRB1_67_32659947_F	32659947	P	1.08E-20	2.38 (1.99-2.86)	3.06E-04	1.55 (1.22-1.96)	2.25E-06	1.86 (1.44-2.41)	5.42E-01	1.11 (0.79-1.57)
SNP_DRB1_32659948_A	32659948	P	1.08E-20	2.38 (1.99-2.86)	3.06E-04	1.55 (1.22-1.96)	2.25E-06	1.86 (1.44-2.41)	5.42E-01	1.11 (0.79-1.57)
HLA_DQB1_0301	32739039	P	2.04E-17	2.22 (1.84-2.66)	3.08E-02	1.31 (1.03-1.68)	9.16E-07	1.93 (1.49-2.51)	4.51E-01	1.15 (0.80-1.64)
rs5000632	32771666	G	4.98E-17	2.11 (1.77-2.52)	1.12E-03	1.42 (1.15-1.75)	5.97E-08	2.03 (1.57-2.62)	2.93E-02	1.41 (1.04-1.92)
rs9357152	32772938	G	4.98E-17	2.11 (1.77-2.52)	1.12E-03	1.42 (1.15-1.75)	5.97E-08	2.03 (1.57-2.62)	2.93E-02	1.41 (1.04-1.92)
rs9394113	32773145	G	4.98E-17	2.11 (1.77-2.52)	1.12E-03	1.42 (1.15-1.75)	5.97E-08	2.03 (1.57-2.62)	2.93E-02	1.41 (1.04-1.92)
AA_DQB1_45_32740702	32740702	E	8.64E-17	2.18 (1.81-2.61)	5.41E-02	1.27 (1.00-1.63)	5.40E-07	1.96 (1.51-2.55)	3.44E-01	1.19 (0.83-1.69)
SNP_DQB1_32737148	32737148	G	8.64E-17	2.18 (1.81-2.61)	5.41E-02	1.27 (1.00-1.63)	5.40E-07	1.96 (1.51-2.55)	3.44E-01	1.19 (0.83-1.69)
SNP_DQB1_32740702	32740702	T	8.64E-17	2.18 (1.81-2.61)	5.41E-02	1.27 (1.00-1.63)	5.40E-07	1.96 (1.51-2.55)	3.44E-01	1.19 (0.83-1.69)
SNP_DQB1_32742309_A	32742309	P	8.64E-17	2.18 (1.81-2.61)	5.41E-02	1.27 (1.00-1.63)	5.40E-07	1.96 (1.51-2.55)	3.44E-01	1.19 (0.83-1.69)
rs9378125	32787710	G	9.33E-17	2.10 (1.76-2.50)	1.51E-03	1.41 (1.14-1.73)	5.97E-08	2.03 (1.57-2.62)	2.93E-02	1.41 (1.04-1.92)
SNP_DRB1_32659973_C	32659973	P	1.71E-16	2.16 (1.80-2.59)	7.28E-02	1.25 (0.98-1.61)	8.22E-05	1.70 (1.31-2.21)	5.59E-01	0.90 (0.62-1.30)

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SNP_DRB1_32659926_CT	32659926	P	4.44E-08	0.56 (0.46-0.69)	4.25E-03	0.73 (0.58-0.90)	2.86E-04	0.58 (0.43-0.78)	9.94E-02	0.77 (0.56-1.05)
rs3134930	32299598	A	5.00E-08	1.61 (1.36-1.91)	9.00E-01	0.99 (0.80-1.22)	7.58E-06	1.79 (1.39-2.31)	1.24E-01	1.26 (0.94-1.69)

For Peer Review

Supplementary Table S5. Amino acid positions associated with systemic sclerosis at the genome-wide significance level ($p < 5 \times 10^{-8}$) after omnibus test in the Iranian and the Turkish cohorts. Abbreviations: HLA: human leucocyte antigen; LRT: likelihood ratio test.

HLA molecule	Amino acid position	Center codon position	Tested Alleles	Iran		Turkey	
				P_{LRT} (unconditioned)	P_{LRT} conditioned on DR β 1 position 58	P_{LRT} (unconditioned)	P_{LRT} conditioned on DR β 1 position 58
DR β 1	58	32659974	2	6.24E-24	NA	4.96E-08	NA
DR β 1	67	32659947	3	5.76E-22	4.18E-02	6.19E-06	8.40E-01
DQ β 1	45	32740702	2	1.14E-17	4.67E-01	3.68E-07	4.15E-01
DQ β 1	55	32740672	3	1.25E-16	1.59E-02	6.95E-03	2.72E-01
DQ β 1	140	32737868	2	2.47E-16	3.68E-02	3.97E-03	4.05E-01
DQ β 1	182	32737742	2	2.47E-16	3.68E-02	3.97E-03	4.05E-01
DP β 1	76	33156640	3	8.06E-14	1.57E-13	8.40E-03	3.93E-03
DQ β 1	38	32740723	2	2.03E-13	1.46E-02	3.58E-03	7.30E-01
DR β 1	70	32659938	3	2.09E-13	3.89E-03	7.32E-04	1.02E-02
DQ α 1	40	32717170	2	2.03E-12	6.52E-01	3.49E-05	6.37E-01
DQ α 1	51	32717203	2	2.03E-12	6.52E-01	3.49E-05	6.37E-01
DQ β 1	30	32740747	3	8.83E-12	1.95E-02	4.23E-03	6.00E-01
DP β 1	35	33156517	3	9.00E-12	1.93E-12	9.92E-02	5.92E-02
DQ β 1	167	32737787	2	1.13E-11	7.83E-02	4.71E-06	4.03E-01
DQ α 1	53	32717209	3	1.48E-11	7.69E-01	2.17E-05	1.34E-01
DQ α 1	50	32717200	3	1.48E-11	7.69E-01	2.17E-05	1.34E-01
DQ β 1	13	32740798	2	2.23E-11	1.78E-01	5.52E-06	5.24E-01
DQ α 1	75	32717275	2	5.45E-11	7.91E-02	8.77E-06	5.24E-01
DQ α 1	156	32717931	2	5.45E-11	7.91E-02	8.77E-06	5.24E-01
DQ α 1	107	32717784	2	5.45E-11	7.91E-02	8.77E-06	5.24E-01
DQ α 1	161	32717946	2	5.45E-11	7.91E-02	8.77E-06	5.24E-01
DQ α 1	163	32717952	2	5.45E-11	7.91E-02	8.77E-06	5.24E-01

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DQ α 1	47	32717191	4	8.25E-11	9.01E-01	8.36E-05	2.51E-01
DR β 1	37	32660037	5	1.64E-10	3.59E-01	1.02E-04	1.16E-02
DQ β 1	26	32740759	3	1.71E-10	3.65E-01	1.95E-05	5.19E-01
DR β 1	32	32660052	2	3.52E-10	1.80E-02	5.35E-04	1.50E-01
DQ β 1	74	32740615	3	4.33E-10	2.13E-02	1.48E-02	5.51E-01
DQ α 1	175	32717988	3	4.57E-10	2.12E-01	6.91E-06	1.31E-01
DQ β 1	67	32740636	2	5.46E-10	6.74E-03	1.61E-02	5.03E-01
DQ β 1	66	32740639	2	5.46E-10	6.74E-03	1.61E-02	5.03E-01
DQ β 1	77	32740606	2	8.29E-10	7.81E-02	5.99E-03	7.03E-01
DQ β 1	37	32740726	3	8.37E-10	5.62E-03	3.38E-02	5.97E-01
DQ β 1	75	32740612	2	1.49E-09	1.66E-01	7.26E-03	8.47E-01
DQ β 1	71	32740624	4	1.99E-09	4.06E-02	3.62E-02	7.41E-01
DR β 1	10	32660118	3	2.37E-09	2.16E-03	7.98E-02	4.95E-01
DQ β 1	47	32740696	2	4.13E-08	5.52E-03	1.34E-02	3.12E-01
DQ β 1	46	32740699	2	4.13E-08	5.52E-03	1.34E-02	3.12E-01
DQ β 1	28	32740753	2	4.13E-08	5.52E-03	1.34E-02	3.12E-01
DQ β 1	52	32740681	2	4.13E-08	5.52E-03	1.34E-02	3.12E-01

Supplementary Table S6. Comparative of the results obtained in Turkish population by Carmona *et al* and our GWAS in four of the most relevant SSc hits.

Abbreviations: SNP: single nucleotide polymorphism; OR: odds ratio; GWAS: genome-wide association study.

SNP	Gene	Study	p value	OR
rs10488631	IRF5-TNPO3	Turkish GWAS	3.05E-03	1.66
		Carmona <i>et al</i>	1.32E-05	1.76
rs3821236	STAT4	Turkish GWAS	3.60E-02	1.34
		Carmona <i>et al</i>	6.50E-02	1.21
rs9373839	ATG5	Turkish GWAS	8.86E-01	1.02
		Carmona <i>et al</i>	6.72E-01	1.06
rs2056626	CD247	Turkish GWAS	6.93E-03	0.71
		Carmona <i>et al</i>	2.20E-03	0.75