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Supplementary Information for

HLA and antibodies define scleroderma subtypes and risk in African and European Americans and suggest a role for molecular mimicry

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Supporting Information Text

Supplemental Materials and Methods

African American cases and controls. AA patients with SSc were enrolled in the GRASP consortium from 23 academic centers in the US.

GRASP Centers

- National Human Genome Research Institute (NHGRI) & National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH)
- Johns Hopkins University
- University of Texas-Houston
- University of Pittsburgh
- Georgetown University
- Medical University of South Carolina
- Northwestern University
- University of Michigan
- Rutgers University
- Hospital for Special Surgery, Cornell University
- Tulane University
- Emory University
- University of California San Francisco
- University of Pennsylvania
- University of Alabama at Birmingham
- George Washington University
- Stanford University
- University of Chicago
- Columbia University
- New York University
- Boston University
- University of California Los Angeles
- Henry Ford Hospital, Detroit, Michigan
- University of Rochester

Only unrelated individuals were included as controls. Sera obtained from controls were tested for antinuclear antibodies (ANAs) by indirect immunofluorescence, and only those with a titer of <1:80 were included in this study. DNA was extracted from samples of whole blood or saliva.

Autoantibody Testing. Sera from the AA SSc patients were tested by a line immunoassay for systemic sclerosis profile autoantibodies (Euroimmun Euroline profile kit, Lübeck, Germany). For the European ancestry SSc patients, reported autoantibody data was extracted from dbGaP accession phs000357.v1.p1. Out of the 115 patients who were ATA+ only 1 was positive for ACA. More globally, 468 of the 723 tested sera (65%) were positive for a SSc-specific autoantibody (ACA, ATA or ARA) and only 8 of those 468 (1.7%) were positive for two autoantigens.

Genotyping. The AA SSc cases and controls were genotyped with the Illumina Infinium Multi-Ethnic Global Array kit. All included samples had call rate greater than 95%. Markers with call rate less than 95%, minor allele frequency less than 0.01, or controls that deviated from Hardy-Weinberg equilibrium with P less than 10^{-5} were excluded. High quality genotypes were imputed using the Michigan Imputation Server and the required 6,114 markers submitted to the HLA*IMP:03 server for HLA imputation. The European ancestry samples were genotyped on Illumina Human610-Quadv1_B chip and the same quality controls were executed separately on the genotypes from each study and then the samples were combined and only markers that were present in all the studies were retained. Samples were also checked for relatedness by an analysis of identity by descent of LD pruned ($r^2 < 0.5$) genotypes and no pairs were allowed with pi-hat greater than 0.085.

Principal Components Analysis (PCA). For the two ancestral populations, PCA was used to evaluate the genetic similarity of the cases with the controls, to remove outliers, and to correct for residual dissimilarity separately. LD-pruned data were used to calculate the top ten principal components for each sample. Two dimensional plots of the PCs allowed removal of outliers. Two dimensional plots of the first two PCs of the cases and the controls included in each study are shown in Supplementary Figure S1.

HLA Imputation.

African American cases and controls. We selected the HLA*IMP:03 tool to perform *HLA* imputation in the AA samples, because it has a multi-ethnic reference panel of 10,561 individuals that includes 568 individuals of African ancestry (1). We extracted genotypes of 19,038 markers that passed quality control from the greater *MHC* region (chromosome 6: 20,000,000 – 40,000,000 on GRCh37/hg19) and used the Michigan Imputation Server to perform haplotype phasing and SNP imputation using Eagle and the 1000G Phase 3 v5 reference (2). We then submitted the phased genotypes of the required 6,114 markers to the HLA*IMP:03 Server, which imputed two two-field (i.e., four-digit) classical *HLA* alleles of 11 *HLA* region genes for each individual. We used available whole exome sequence for 763 of the AA samples to determine their *HLA* alleles with a software tool that performs alignments to a population reference graph of the *HLA* region (HLA*PRG:LA) allowing comparison of the HLA*IMP:03 imputed alleles with the sequence based alleles (3).

European American cases and controls. We extracted genotypes of 2,690 SNPs that passed quality control in all the European ancestry datasets from the greater *MHC* region and used SNP2HLA and a mainly European ancestry reference of 5,225 individuals from the Type I Diabetes Consortium to impute classical *HLA* alleles and polymorphic amino acids of the HLA proteins (4).

***HLA* Association and Conditional Analysis.** The HLA*IMP:03 imputed alleles for each gene were recoded as individual markers, each with two presence or absence alleles (PP, PA, or AA), matching the SNP2HLA imputation output. Alleles with frequency less than 0.01 were omitted. For *HLA* allele association, a logistic regression analysis was performed under a dominant model, encoding AA genotypes=0 and AP and PP genotypes=1. A dominant model was applied for analysis of *HLA* alleles because it is consistent with the method classically used for identifying *HLA* alleles associated with different human diseases (5). It is also consistent with the importance of presence or absence of a molecule endowing capability to bind and present specific peptide antigens. Regressions were corrected for genetic dissimilarity between the cases and the controls by including the top 10 PCs as covariates. To account for strong LD in the region, independent associations were identified by performing conditional analysis and at each level the strongest association accepted, and the scan rerun with all the previous 'accepted' associations included as covariates. This was done until p-value statistical significance threshold was reached. The total number of classical *HLA* alleles tested for association were 138 in both the populations and there were 5 analysis conducted. Thus a Bonferroni's multiple test corrected significance threshold of $P < 0.000072$ was used for association analysis.

Amino Acid Analysis. For the HLA*IMP:03 imputed data, the genotypes of all the polymorphic amino acids of the HLA proteins were extracted from the IPD-IMGT/HLA Database according to the two alleles specified for each imputed gene and each polymorphic amino acid marker was coded for absence or presence genotypes, AA, AP, or PP (6). The SNP2HLA output included similarly encoded P/A genotypes for each of the polymorphic amino acids. Amino acid associations with SSc were evaluated with a dominant model logistic regression analysis as done for the *HLA* alleles. Amino acids with frequency less than 0.01 were omitted. To account for strong LD in the region, independent associations were identified by performing conditional analysis and at each level the strongest association accepted, and the scan rerun with all the previous 'accepted' associations included as covariates. This was done until p-value statistical significance threshold was reached. The p-value threshold was set as $P< 0.000013$ based on 800 amino acids tested across both population samples, multiplied by 5 sets of analysis.

***HLA* Alpha-Beta Chain Pair Analysis.** The non-polymorphic HLA-DR alpha chain combines with HLA-DRB1 alleles, thus disease-associated DR1 alpha/beta combinations are defined by the association of DRB1 alleles. However, HLA-DQ1 and HLA-DP1 molecules have polymorphic alpha and beta chains, therefore the association of DQA1/DQB1 and DPA1/DPB1 allele pairs are relevant to disease association. To identify SSc-associated HLA-DQ and -DP alpha and beta chain pairs we performed haplotype association analysis of the *HLA-DQ* and *-DP* genotypes using Haploview and then created new P/A markers for the haplotypes that were analyzed by logistic regression (7).

3D Protein Modeling. Protein Data Bank entries 1a35 for topoisomerase I, 2ipx for fibrillarin, 3nqu for centromere protein A, 6atf for HLA-DR, 1s9v for HLA-DQ, and 3lqz for HLA-DP were obtained and UCSF chimera was used to model the individual amino acid positions. Molecular graphics and analyses performed with UCSF Chimera, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from NIH P41-GM103311 (8).

CART Analysis. Classification and Regression Tree (CART) analysis was performed to explore higher order interactions amongst the HLA alleles (CART 6.0, Salford Systems, San Diego, CA) (9). *HLA* alleles were used as nominal categorical variables to predict the outcome SSc. CART analysis interactively identifies the most powerful variable classifier for SSc and splits the variables into binary trees (presence/absence). The SSc-specific autoantibody subsets of SSc for both the AA and EA populations were analyzed individually and split into successive groups using ten-fold cross-validation and trees were pruned for significance at p-value (P)<0.001 using Pearson's chi-square test or, when appropriate, Fisher's exact test.

Identification of Immunodominant Peptides. The HLA-II peptide groove is open at both ends, thus it can allow peptide binding of varying lengths (10). Predominantly, 13-25 residues long peptides have been found to bind HLA-II in nature with the most abundant having an average peptide length of 15 residues (11–16). Several previous studies have used 15-mer residues as the default peptide length for predicting peptides that will bind to HLA-II molecule (17–22). The default peptide length suggested for the NetMHCIIpan 3.2 server is a 15-mer peptide (23, 24). The NetMHCIIpan 3.2 server was used to predict the binding of 15-mer peptide sequences within the protein of interest (topoisomerase I, fibrillarin, or CENPA/CENPB) to the SSc-associated *MHC* Class II α/β heterodimers within the respective autoantibody subsets. Peptides with a binding affinity $\leq$500nM and observed in two of the SSc-associated *HLA* α/β heterodimers were prioritized as immunodominant peptides (23). The identified peptides were sorted by affinity (IC50 values). For each autoantibody subset, the resulting lists of peptide binders were analyzed for overlap in peptide sequences between the different *HLA* alleles, and peptide sequences were selected if they had moderate binding affinity for both the associated alleles. The prediction values are given as IC50 values in nanomolar (nM). Strong binders are defined as peptides with a binding affinity less than or equal to 50 nM, and moderate binders are those with an affinity greater than 50 nM but less than or equal to 500 nM (23, 25–27).

Molecular Mimicry. The prioritized immunodominant peptide sequences were entered into the NCBI Basic Local Alignment Search Tool Standard Protein BLAST with the organism set to virus (taxid:10239) and human (taxid:9606) to identify homologous sequences in viral and human sequence databases, respectively. Significant homology was defined by an E-value $<$ 0.05 (28). To rule out homology by chance, one hundred 15-mer random sequence peptides were generated using ExPASy from the Swiss Institute of Bioinformatics (SIB) and Sequence Manipulation Suite and compared for homologous sequences in viral sequence database (29, 30). We used an arbitrarily selected 15-mer peptide from serum albumin comprising residues 152-166 as an additional comparator for self-antigen homology (31).

Web Addresses.

- dbGaP: https://www.ncbi.nlm.nih.gov/gap
- HLA-PRG-LA: https://github.com/DiltheyLab/HLA-PRG-LA
- Michigan Imputation Server: https://imputationserver.sph.umich.edu/index.html
- HLA*IMP:03 Server: http://imp.science.unimelb.edu.au/hla/
- SNP2HLA: http://software.broadinstitute.org/mpg/snp2hla/
- The IPD-IMGT/HLA Database: https://www.ebi.ac.uk/ipd/imgt/hla/
- Haploview: https://www.broadinstitute.org/haploview/haploview
- NetMHCIIpan: http://www.cbs.dtu.dk/services/NetMHCIIpan/
- NCBI Protein Blast: https://blast.ncbi.nlm.nih.gov/Blast.cgi?PROGRAM=blastp&PAGE_TYPE=BlastSearch&LINK_LOC=blasthome
- UCSF Chimera: https://www.cgl.ucsf.edu/chimera/
- Random Peptide generators: https://web.expasy.org/randseq/, http://www.bioinformatics.org/sms2/random_protein.html

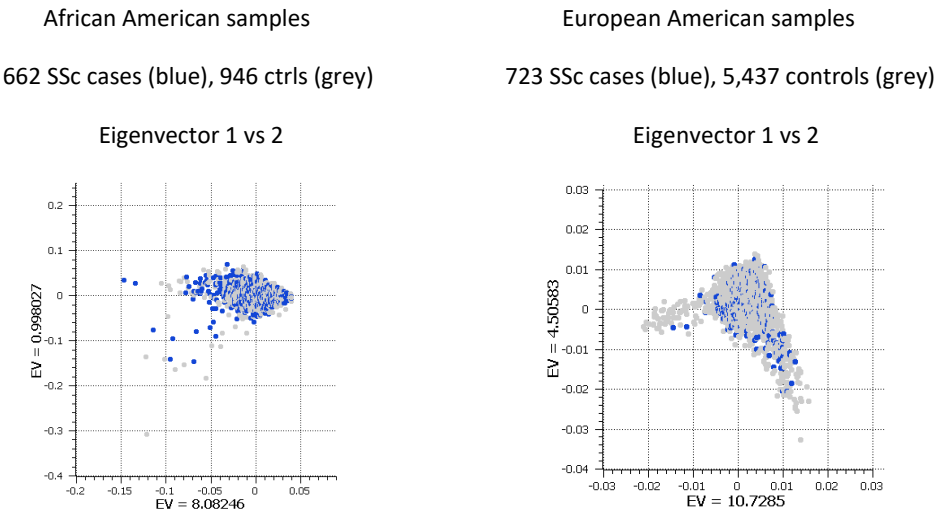


Fig. S1. Principal component analysis (PCA) plots of the African and European American SSc cases and controls included in the study. PCA was performed on LD-pruned data ($r^2 < 0.5$).

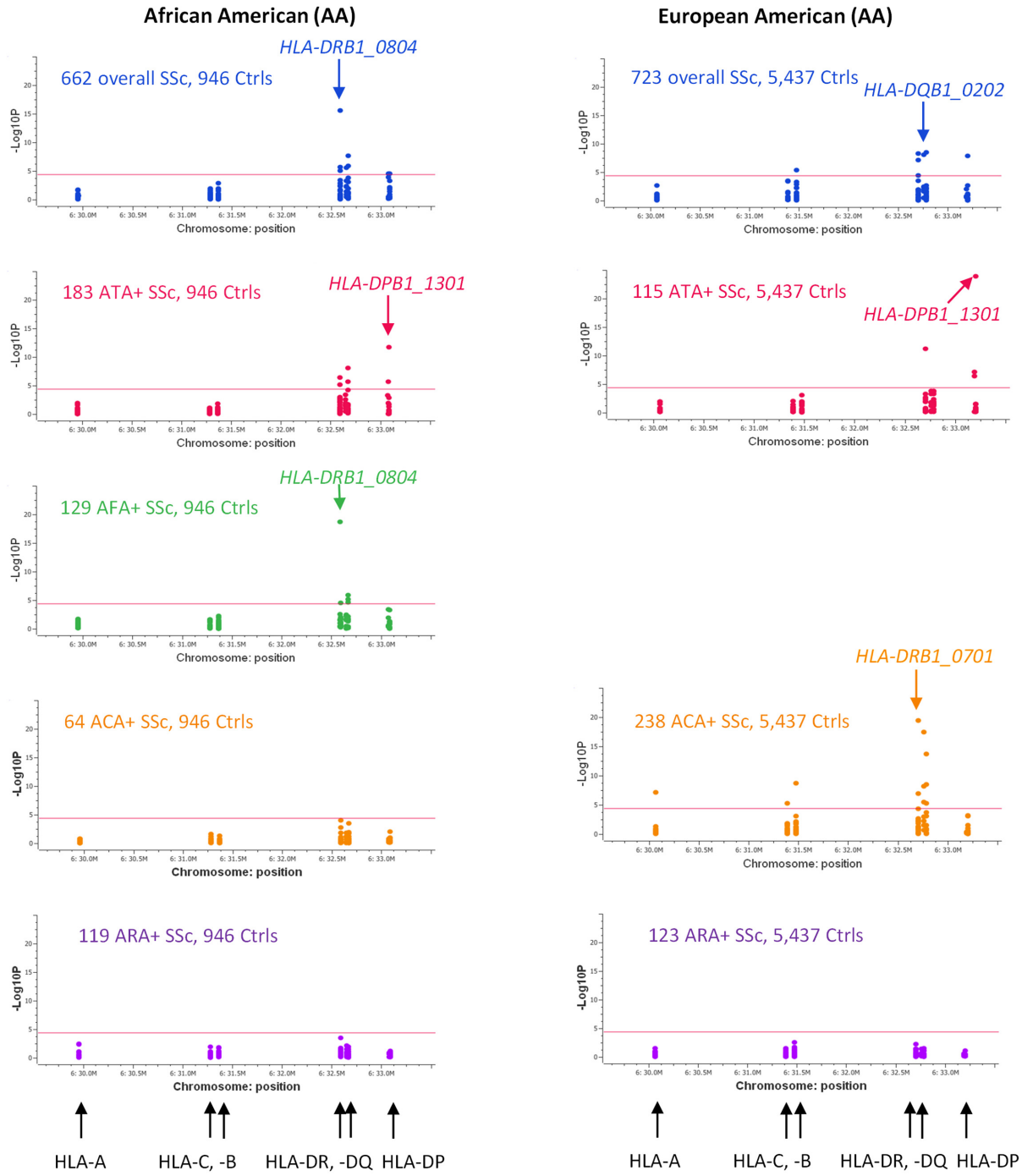
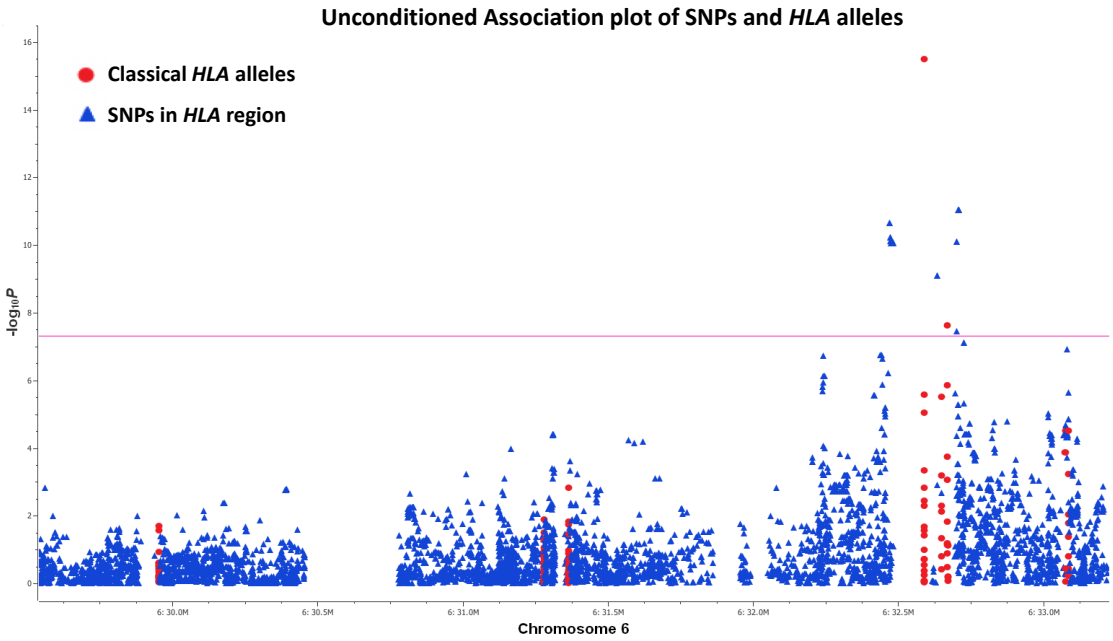


Fig. S2. Association of classical *HLA* alleles with SSc and autoantibody subsets of SSc in African and European Americans. *HLA* imputed classical allele associations in SSc and autoantibody subsets determined in African Americans (left panels) and European Americans (right panels). Common AA haplotype: *HLA-DRB1*08:04/DQA1*05:01/DQB1*03:01*; Common EA haplotypes: *HLA-DRB1*11:04/DQA1*05:01/DQB1*03:01 and HLA-DRB1*07:01/DQA1*02:01/DQB1*02:02.*



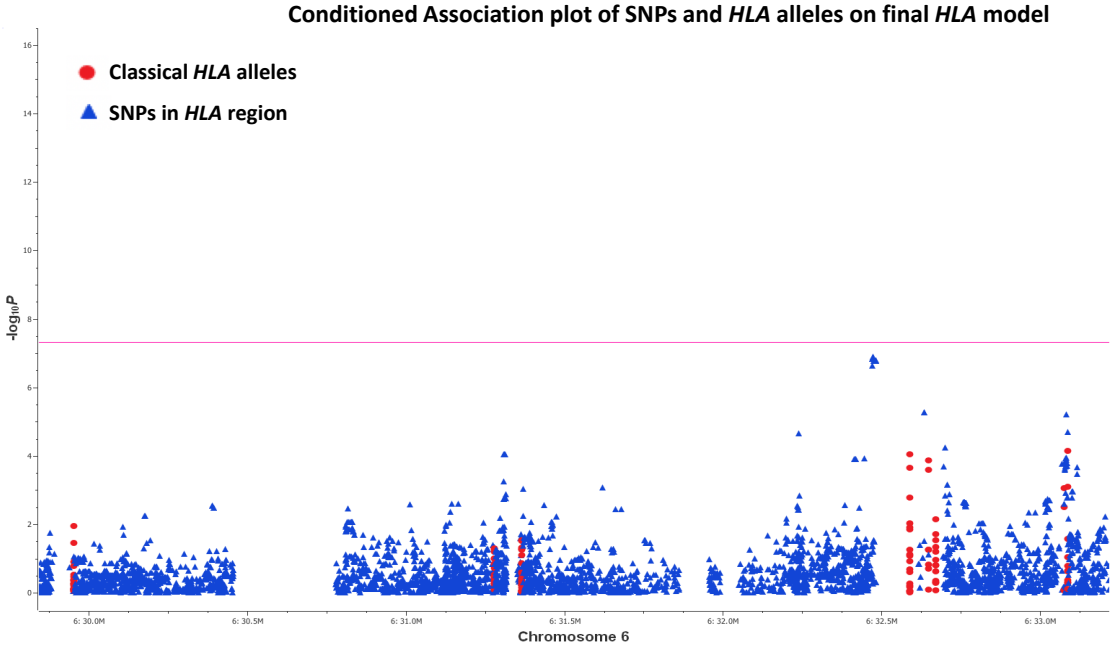


Fig. S3. Association Analysis in African Americans of the *HLA* region SNPs and Classical *HLA* alleles, both Unconditioned and Conditioned on the final *HLA* model, *HLA-DRB1*08:04* and *HLA-DRB1*11:02* alleles. Both analyses corrected for the top 10 Principal Components.

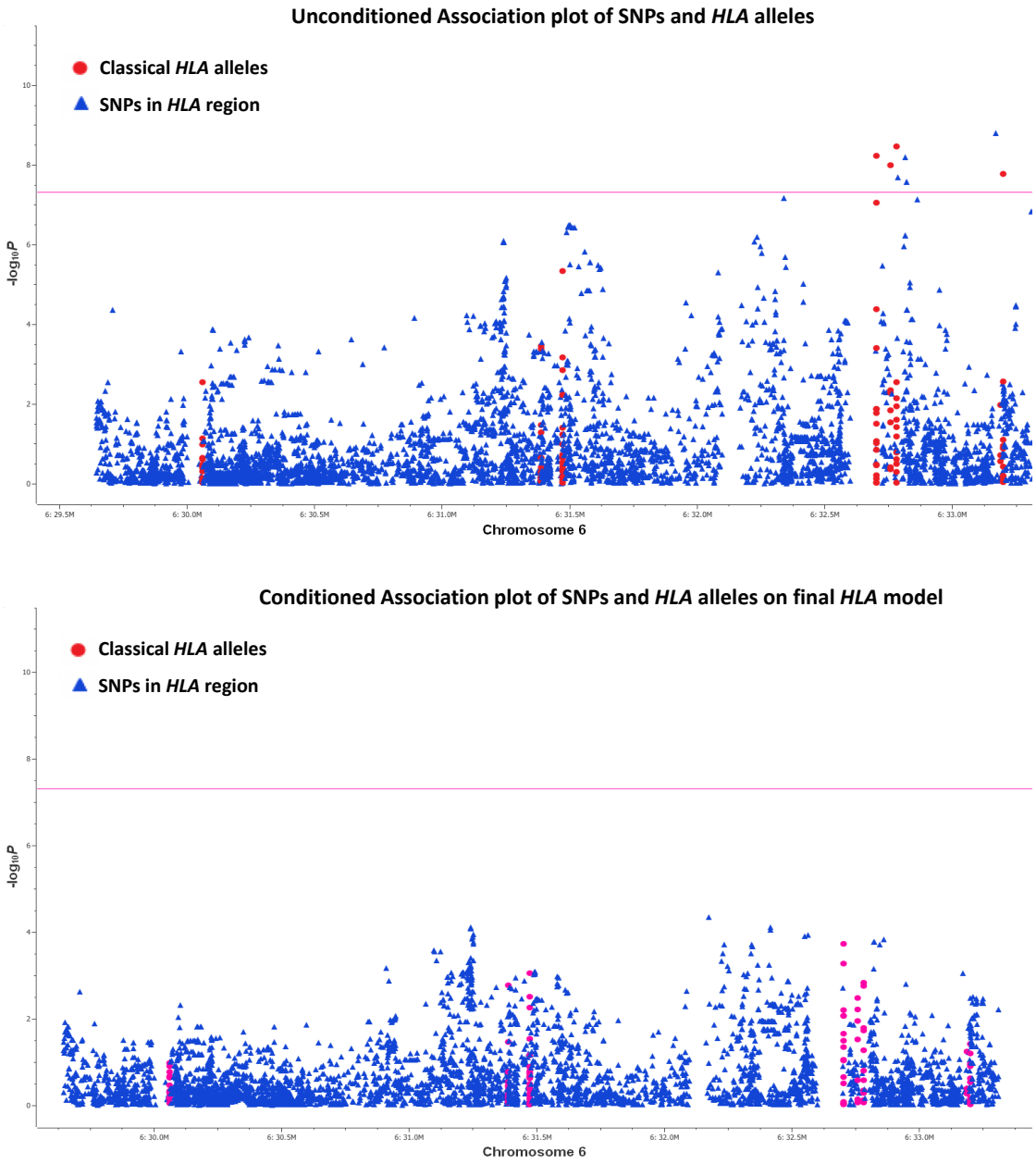


Fig. S4. Association Analysis in European Americans of the *HLA* region SNPs and Classical *HLA* alleles, both Unconditioned and Conditioned on the final *HLA* model, *HLA-DQB1*02:02*, *HLA-DPB1*13:01* and *HLA-DRB1*11:04* alleles. Both analyses corrected for the top 10 Principal Components.

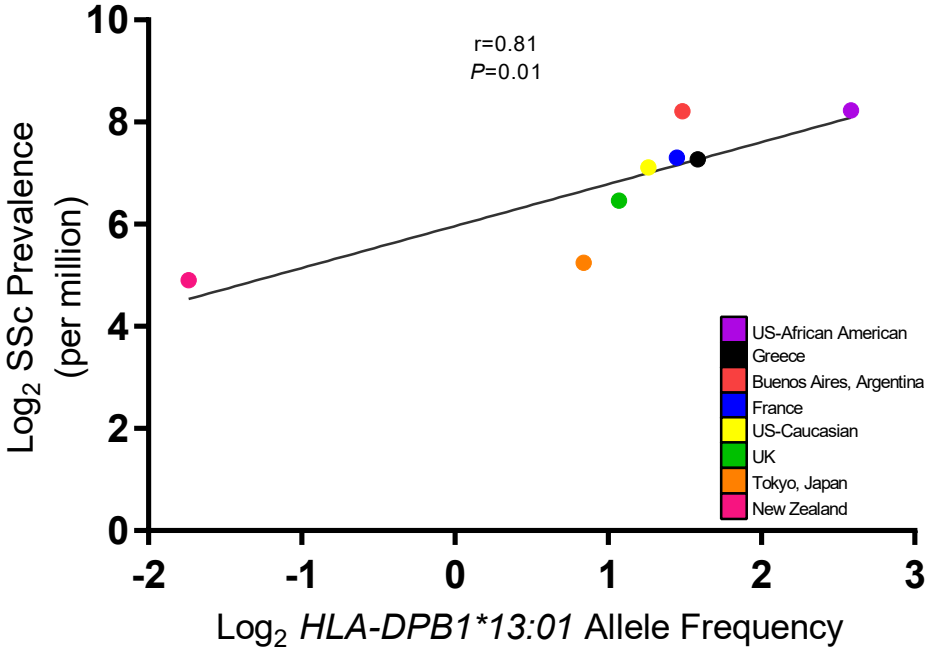


Fig. S5. Population frequency of *HLA-DPB1*13:01* allele and SSc prevalence with outlier removed (see Figure 1).

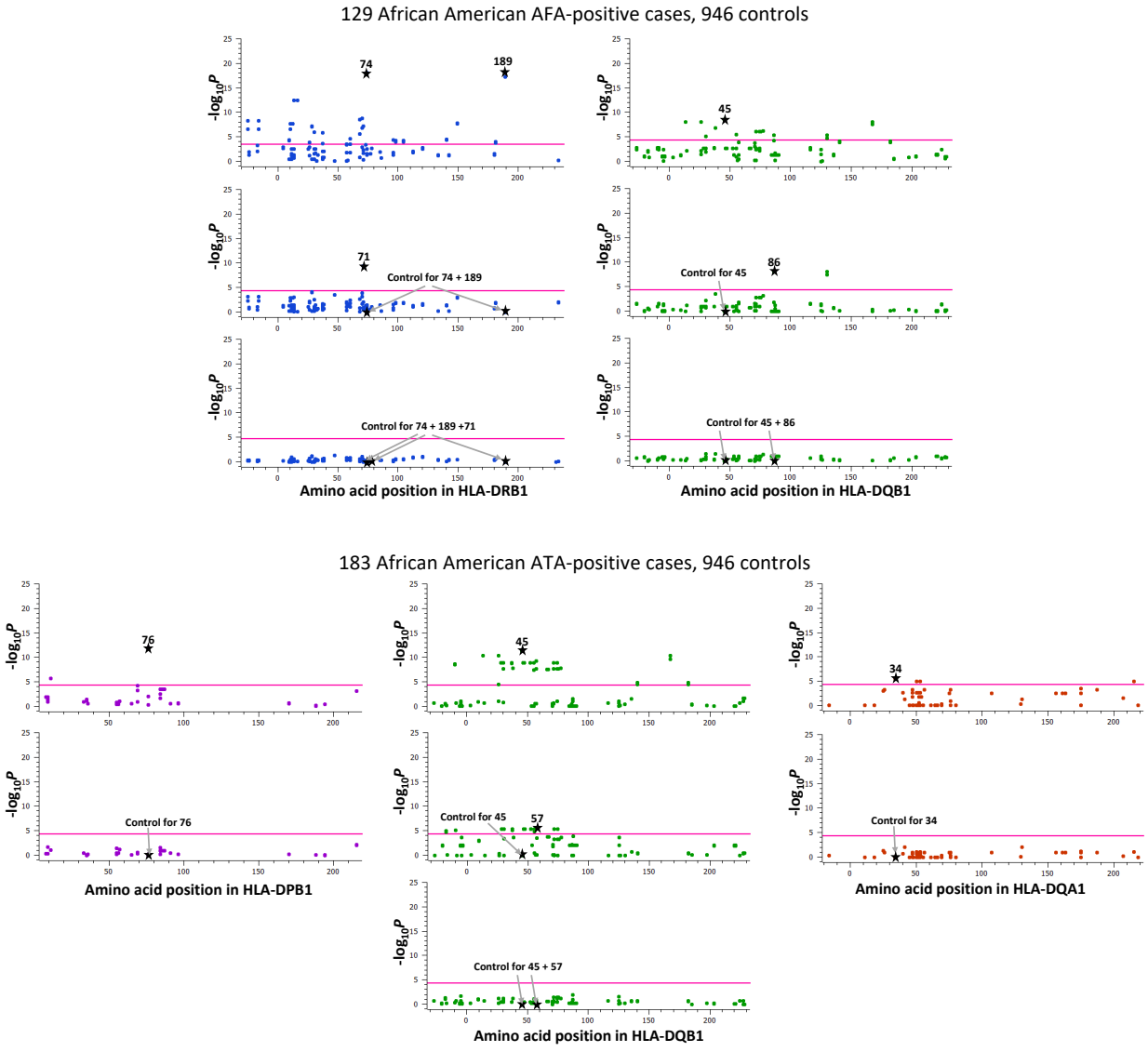


Fig. S6. (A) Logistic regression and conditional analysis of HLA polymorphic amino acids within autoantibody subsets of SSc in African Americans in the AFA+ SSc subset (top) and ATA+ SSc subset (bottom). *(SSc=systemic sclerosis; AFA=anti-fibrillarin antibody; ATA=anti-topoisomerase I antibody)*

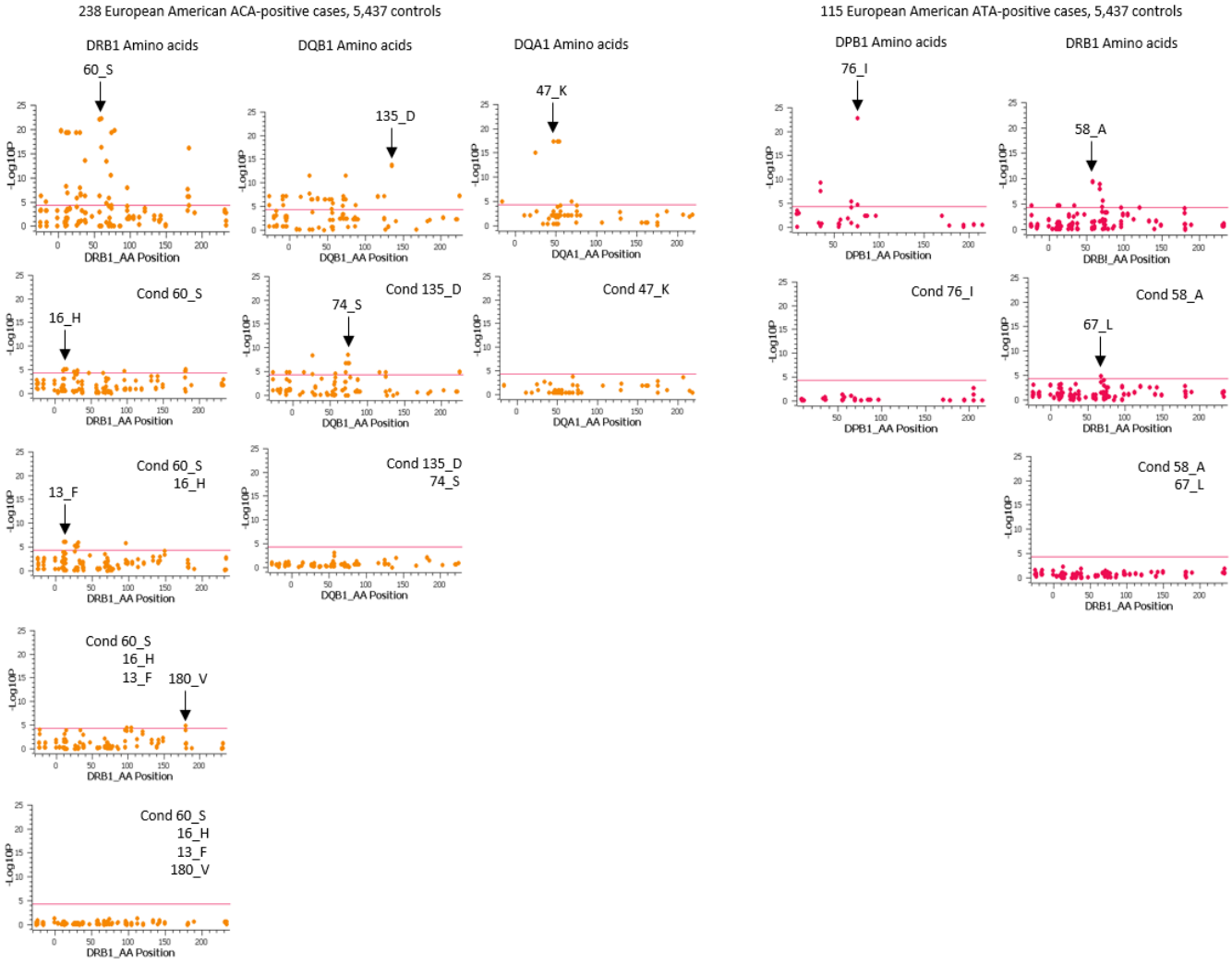


Fig. S6. (B) Logistic regression and conditional analysis of HLA polymorphic amino acids within autoantibody subsets of SSc in European Americans in the ACA+ SSc subset (left) and ATA+ SSc subset (right). *(SSc=systemic sclerosis; ACA=anti-centromere antibody; ATA=anti-topoisomerase I antibody)*

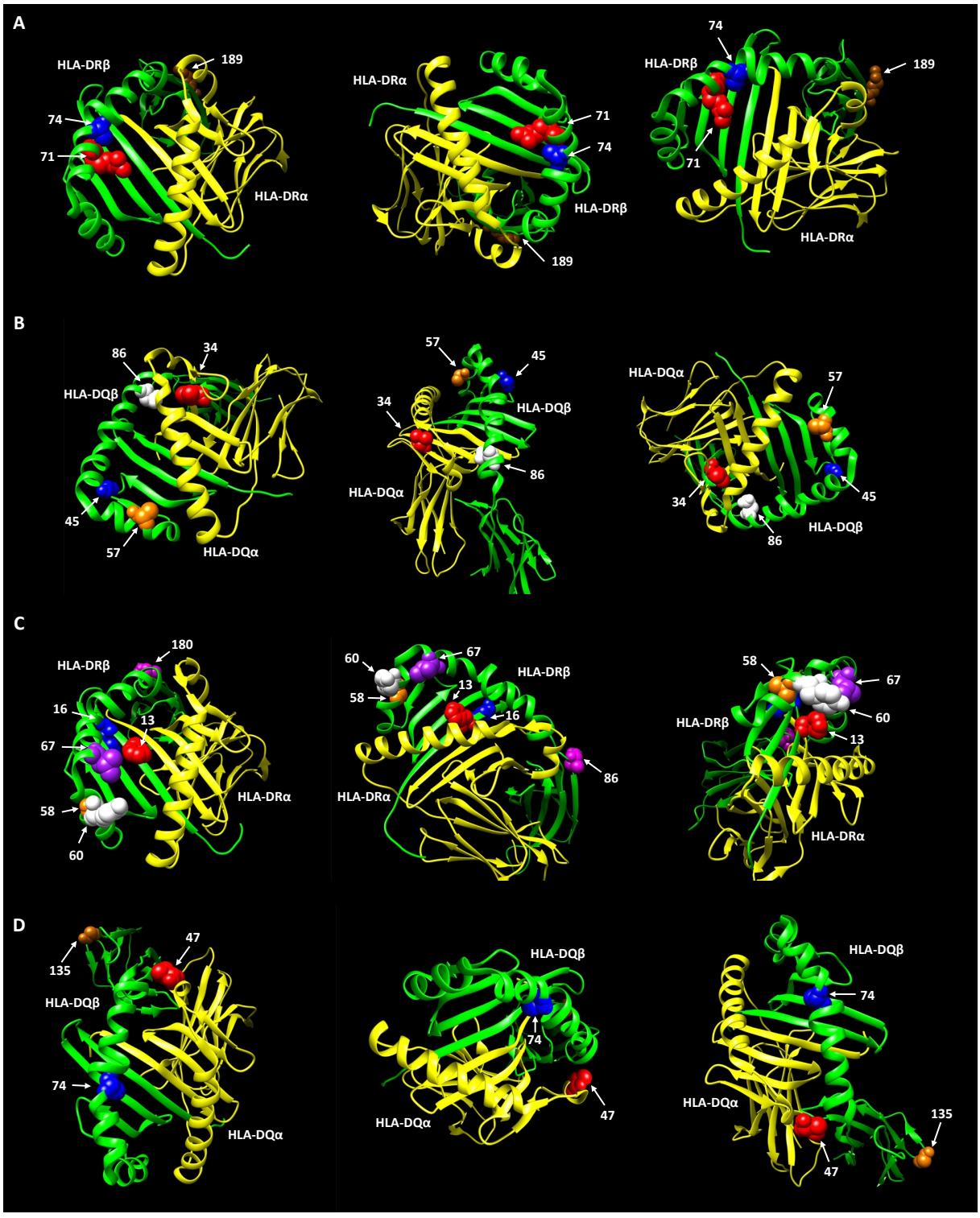


Fig. S7. Ribbon models of the HLA-DR and HLA-DQ proteins with independently associated amino acid residues, based on Protein Data Bank entries 6atf and 1s9v, respectively. (A) 3D model of HLA-DR in three different orientations in order to visualize peptide binding grove and associated amino acid positions in African Americans; (B) 3D model of HLA-DQ in three different orientations in order to visualize peptide binding grove and associated amino acid positions in African Americans; (C) 3D model of HLA-DR in three different orientations in order to visualize peptide binding grove and associated amino acid positions in European Americans; (D) 3D model of HLA-DQ in three different orientations in order to visualize peptide binding grove and associated amino acid positions in European Americans.

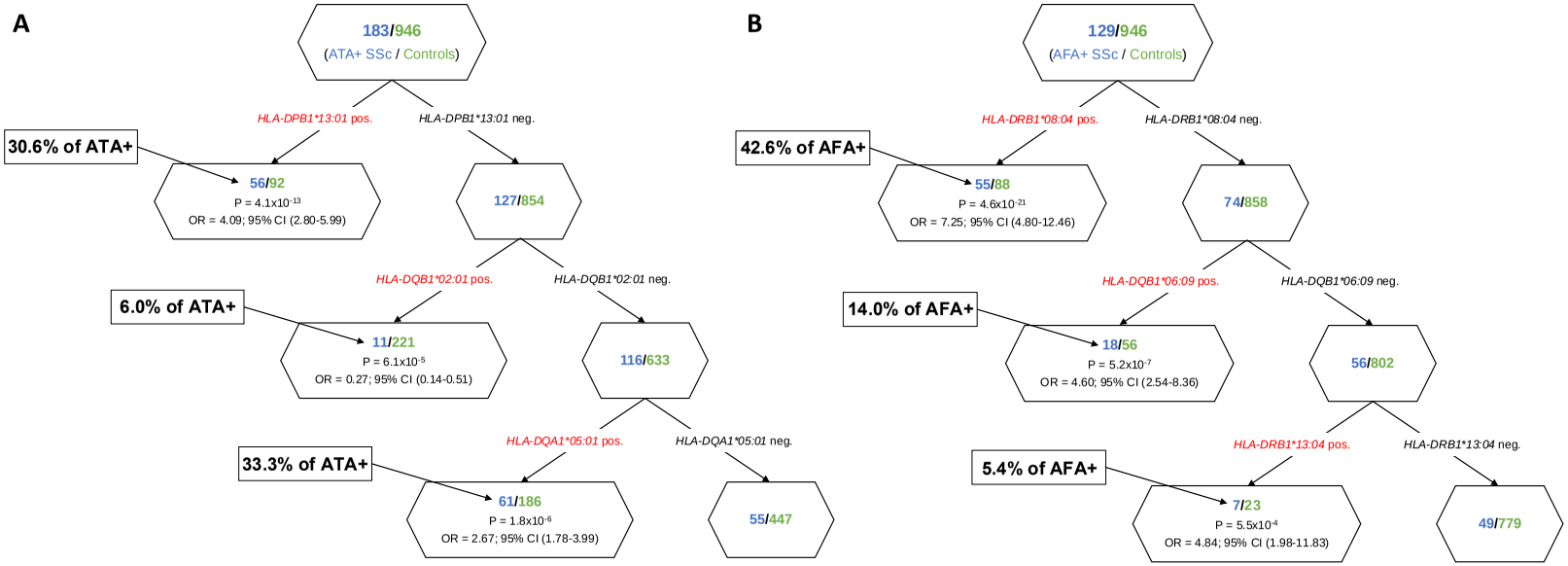


Fig. S8. Classification and regression tree (CART) analysis of (A) African American SSc anti-topoisomerase I autoantibody subset and (B) African American SSc anti-fibrillarin autoantibody subset.

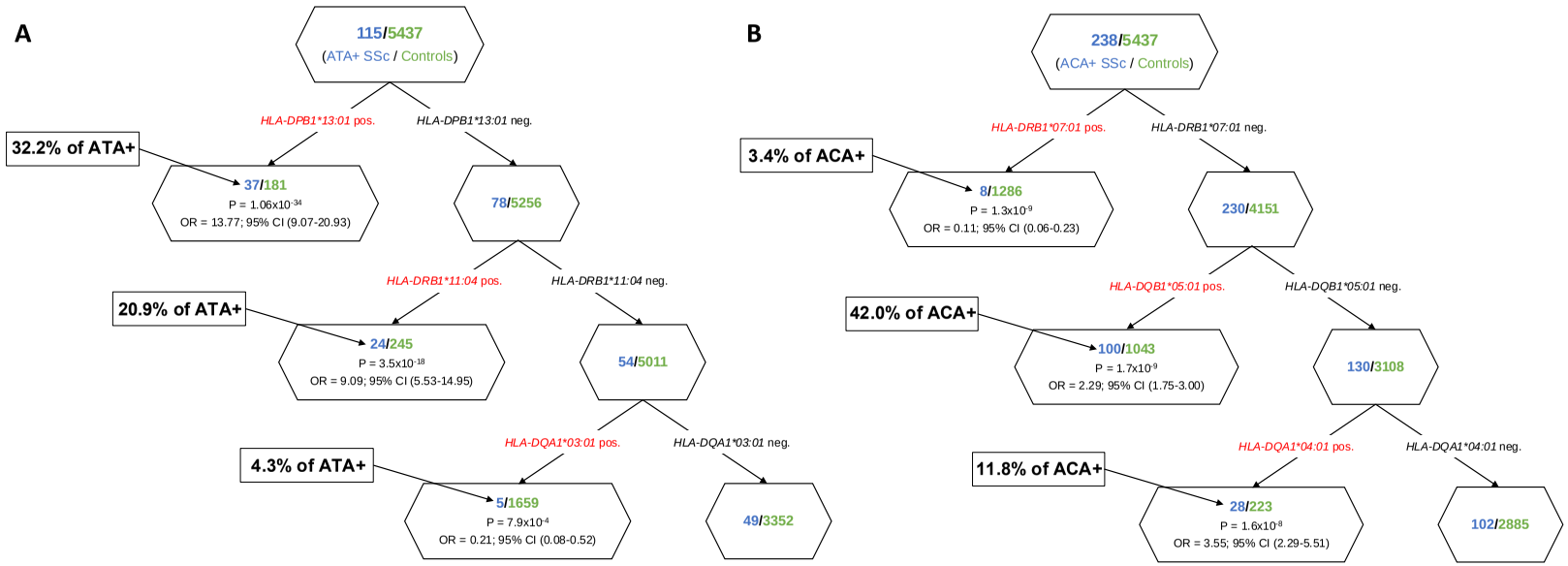


Fig. S9. Classification and regression tree (CART) analysis of (A) European American SSc anti-topoisomerase I autoantibody subset and (B) European American SSc anti-centromere autoantibody subset.

Table S1. European American SSc and control datasets obtained from dbGaP.

Sample Collection	dbGaP Accession Number	# Samples Included
Genome-Wide Association Study in Systemic Sclerosis, cases	phs000357.v1.p1	723
Cohort-Based Genome-Wide Association Study of Glioma (GliomaScan), controls	phs000652.v1.p1	29
GWAS for Genetic Determinants of Bone Fragility, controls	phs000138.v2.p1	714
Cancer Genetic Markers of Susceptibility for Bladder Cancer (CGEMS Bladder), controls	phs000346.v2.p2	1,354
The Breast and Prostate Cancer Cohort Consortium (BPC3), controls	phs000812.v1.p1	2,411
PGRN-RIKEN: Genome-Wide Association Study of Drug-Induced Long-QT Syndrome, controls	phs000331.v1.p1	169
NIA-Late Onset Alzheimer's Disease and National Cell Repository for Alzheimer's Disease Family Study, controls	phs000168.v2.p2	760

Table S2. Sample demographics.

	African Americans	European Americans
Controls		
n	946	5,437
Female, number (%)	502 (53.1)	3333 (61.3)
Male, number (%)	444 (46.9)	2103 (38.7)
SSc patients		
n	662*	723
Female, number (%)	510 (77)	643 (88.9)
Male, number (%)	150 (22.7)	80 (11.1)
Antibodies		
Anti-topoisomerase I, number (%)	183 (27.6)	115 (15.9)
Anti-fibrillarin, number (%)	129 (19.5)	Not Measured
Anti-centromere, number (%)	64 (9.7)	238 (32.9)
Anti-RNA polymerase III, number (%)	119 (18.0)	123 (17.0)

**Two samples had missing gender data.*

Table S3. HLA*IMP:03-imputed allele concordance with sequence-based types of 763 African Americans determined with HLA-PRG-LA.

***HLA* Locus**	**# Types with Frequency > 1%***	**Concordance Rate**
HLA-A	19	98.58%
HLA-B	24	98.62%
HLA-C	15	97.52%
HLA-DRB1	21	99.07%
HLA-DQA1	7	98.13%
HLA-DQB1	12	97.93%
HLA-DPA1	3	95.96%
HLA-DPB1	11	99.03%

**In the HLA-PRG-LA data.*

Table S4. *HLA* allele frequencies in African Americans.

Allele	Frequency Cases (%) n=662	Frequency Controls (%) n=946
*HLA-A*01:01*	4.0	4.5
*HLA-A*02:01*	13.0	12.0
*HLA-A*02:02*	3.4	3.4
*HLA-A*02:05*	2.2	2.3
*HLA-A*03:01*	8.5	7.4
*HLA-A*11:01*	1.1	1.3
*HLA-A*23:01*	12.1	10.4
*HLA-A*24:02*	1.6	2.6
*HLA-A*26:01*	1.4	1.4
*HLA-A*29:02*	2.8	3.7
*HLA-A*30:01*	6.8	6.6
*HLA-A*30:02*	5.5	6.1
*HLA-A*32:01*	1.0	1.5
*HLA-A*33:01*	3.0	2.6
*HLA-A*33:03*	5.9	5.5
*HLA-A*34:02*	3.2	3.5
*HLA-A*36:01*	2.6	2.4
*HLA-A*66:01*	1.4	1.7
*HLA-A*68:01*	4.3	4.6
*HLA-A*74:01*	4.4	5.3
*HLA-B*07:02*	6.5	7.9
*HLA-B*08:01*	4.9	4.2
*HLA-B*14:02*	2.0	2.1
*HLA-B*15:01*	0.8	1.6
*HLA-B*15:03*	5.7	5.3
*HLA-B*15:10*	3.0	3.4
*HLA-B*15:16*	2.0	1.3
*HLA-B*18:01*	2.9	3.4
*HLA-B*35:01*	7.2	7.5
*HLA-B*40:01*	1.1	1.0
*HLA-B*42:01*	5.3	5.8
*HLA-B*44:02*	1.4	1.3
*HLA-B*44:03*	5.0	5.5
*HLA-B*45:01*	4.6	4.7
*HLA-B*49:01*	3.0	3.0
*HLA-B*51:01*	3.9	2.6
*HLA-B*53:01*	15.0	11.7
*HLA-B*57:01*	1.1	1.2
*HLA-B*57:03*	2.1	3.5
*HLA-B*58:01*	4.7	4.3
*HLA-B*58:02*	4.3	4.2
*HLA-B*81:01*	1.1	1.7

(continued on next page)

Table S4. *HLA* allele frequencies in African Americans (continued).

Allele	Frequency Cases (%) n=662	Frequency Controls (%) n=946
*HLA-C*02:02*	6.0	6.2
*HLA-C*02:10*	1.7	1.2
*HLA-C*03:02*	2.2	1.8
*HLA-C*03:03*	0.9	1.4
*HLA-C*03:04*	5.6	4.9
*HLA-C*04:01*	23.0	20.3
*HLA-C*05:01*	2.7	2.6
*HLA-C*06:02*	8.8	9.4
*HLA-C*07:01*	11.9	13.1
*HLA-C*07:02*	6.8	8.1
*HLA-C*08:02*	3.1	3.8
*HLA-C*12:03*	1.0	1.8
*HLA-C*14:02*	2.3	1.8
*HLA-C*15:05*	0.8	1.0
*HLA-C*16:01*	10.5	8.6
*HLA-C*17:01*	6.9	7.1
*HLA-C*18:01*	2.3	3.2
*HLA-DRB1*01:01*	2.1	2.1
*HLA-DRB1*01:02*	2.5	3.9
*HLA-DRB1*03:01*	4.8	7.7
*HLA-DRB1*04:01*	1.1	1.7
*HLA-DRB1*04:05*	0.8	2.0
*HLA-DRB1*07:01*	5.8	10.7
*HLA-DRB1*08:04*	12.7	4.8
*HLA-DRB1*09:01*	2.5	2.5
*HLA-DRB1*10:01*	1.1	1.6
*HLA-DRB1*11:01*	9.4	7.9
*HLA-DRB1*11:02*	7.3	3.8
*HLA-DRB1*12:01*	2.5	3.8
*HLA-DRB1*13:01*	3.8	4.4
*HLA-DRB1*13:02*	8.8	7.1
*HLA-DRB1*13:03*	2.9	3.5
*HLA-DRB1*13:04*	3.1	1.3
*HLA-DRB1*14:01*	1.1	2.3
*HLA-DRB1*15:01*	3.0	3.2
*HLA-DRB1*15:03*	13.1	12.6
*HLA-DRB1*16:02*	1.4	1.4
*HLA-DQA1*01:01*	9.9	13.3
*HLA-DQA1*01:02*	33.9	31.1
*HLA-DQA1*01:03*	1.9	2.4
*HLA-DQA1*02:01*	5.9	10.7
*HLA-DQA1*03:01*	7.9	10.5
*HLA-DQA1*04:01*	12.2	10.1
*HLA-DQA1*05:01*	28.0	21.5
*HLA-DQB1*02:01*	9.1	13.5
*HLA-DQB1*02:02*	4.2	7.5
*HLA-DQB1*03:01*	20.5	13.6
*HLA-DQB1*03:02*	2.3	3.3
*HLA-DQB1*03:03*	2.0	2.5
*HLA-DQB1*03:19*	10.1	4.5
*HLA-DQB1*04:02*	6.3	7.7
*HLA-DQB1*05:01*	12.4	14.5
*HLA-DQB1*05:03*	0.9	1.9
*HLA-DQB1*06:02*	20.5	20.2
*HLA-DQB1*06:03*	1.2	1.4
*HLA-DQB1*06:04*	2.1	2.0
*HLA-DQB1*06:09*	4.4	3.3

(continued on next page)

Table S4. *HLA* allele frequencies in African Americans (continued).

Allele	Frequency Cases (%) n=662	Frequency Controls (%) n=946
*HLA-DPA1*01:03*	32.6	39.1
*HLA-DPA1*02:01*	40.0	31.0
*HLA-DPA1*02:02*	15.3	16.3
*HLA-DPA1*03:01*	11.6	12.4
*HLA-DPB1*01:01*	32.2	28.5
*HLA-DPB1*02:01*	12.7	13.2
*HLA-DPB1*03:01*	5.3	5.3
*HLA-DPB1*04:01*	8.4	10.9
*HLA-DPB1*04:02*	11.3	12.7
*HLA-DPB1*11:01*	1.7	3.1
*HLA-DPB1*13:01*	9.0	5.1
*HLA-DPB1*17:01*	8.9	8.1
*HLA-DPB1*18:01*	4.2	7.0
*HLA-DPB1*40:01*	1.9	1.2
*HLA-DPB1*85:01*	1.1	1.5

Table S5. *HLA* allele frequencies in European Americans.

Allele	Frequency Cases (%) n=723	Frequency Controls (%) n=5437
*HLA-A*01:01*	16.9	16.6
*HLA-A*02:01*	28.7	28.5
*HLA-A*03:01*	14.3	14.9
*HLA-A*11:01*	6.3	5.9
*HLA-A*23:01*	1.7	1.9
*HLA-A*24:02*	9.5	8.1
*HLA-A*25:01*	2.0	2.3
*HLA-A*26:01*	3.3	2.7
*HLA-A*29:02*	2.1	3.5
*HLA-A*30:01*	0.9	1.1
*HLA-A*31:01*	2.6	2.6
*HLA-A*32:01*	3.2	3.7
*HLA-A*68:01*	2.8	3.3
*HLA-B*07:02*	12.3	14.5
*HLA-B*08:01*	14.5	12.2
*HLA-B*13:02*	1.2	2.1
*HLA-B*14:02*	2.9	2.4
*HLA-B*15:01*	6.2	6.9
*HLA-B*18:01*	5.5	4.0
*HLA-B*27:05*	4.1	4.1
*HLA-B*35:01*	7.8	5.7
*HLA-B*35:02*	1.4	0.5
*HLA-B*35:03*	1.2	1.5
*HLA-B*37:01*	1.2	1.5
*HLA-B*38:01*	1.4	1.6
*HLA-B*39:01*	1.7	1.3
*HLA-B*40:01*	5.5	5.7
*HLA-B*40:02*	1.5	1.1
*HLA-B*44:02*	9.5	9.7
*HLA-B*44:03*	2.6	4.9
*HLA-B*49:01*	0.9	1.4
*HLA-B*51:01*	5.4	4.7
*HLA-B*55:01*	1.7	1.8
*HLA-B*57:01*	2.6	3.4
*HLA-C*01:02*	3.6	3.6
*HLA-C*02:02*	4.7	4.4
*HLA-C*03:03*	5.2	5.8
*HLA-C*03:04*	8.0	8.2
*HLA-C*04:01*	12.1	10.2
*HLA-C*05:01*	9.0	9.6
*HLA-C*06:02*	6.4	8.7
*HLA-C*07:01*	18.7	16.2
*HLA-C*07:02*	13.7	15.5
*HLA-C*07:04*	1.9	1.5
*HLA-C*08:02*	3.4	3.5
*HLA-C*12:03*	4.9	4.3
*HLA-C*14:02*	1.5	1.3
*HLA-C*15:05*	2.1	2.0
*HLA-C*16:01*	1.9	3.5

(continued on next page)

Table S5. *HLA* allele frequencies in European Americans (continued).

Allele	Frequency Cases (%) n=723	Frequency Controls (%) n=5437
*HLA-DRB1*01:01*	12.7	9.1
*HLA-DRB1*01:02*	1.1	0.9
*HLA-DRB1*01:03*	0.8	1.4
*HLA-DRB1*03:01*	14.0	12.1
*HLA-DRB1*04:01*	9.1	10.0
*HLA-DRB1*04:04*	5.1	4.1
*HLA-DRB1*07:01*	8.0	12.7
*HLA-DRB1*08:01*	3.4	2.3
*HLA-DRB1*09:01*	0.6	1.0
*HLA-DRB1*11:01*	5.5	5.2
*HLA-DRB1*11:04*	5.3	2.4
*HLA-DRB1*12:01*	0.8	1.5
*HLA-DRB1*13:01*	4.6	6.3
*HLA-DRB1*13:02*	4.4	4.3
*HLA-DRB1*14:01*	1.1	2.5
*HLA-DRB1*15:01*	12.2	14.6
*HLA-DRB1*16:01*	1.7	1.4
*HLA-DQA1*01:01*	17.4	14.5
*HLA-DQA1*01:02*	19.3	21.3
*HLA-DQA1*01:03*	4.9	6.6
*HLA-DQA1*02:01*	8.4	13.1
*HLA-DQA1*03:01*	17.8	17.8
*HLA-DQA1*04:01*	4.2	2.7
*HLA-DQA1*05:01*	27.7	23.6
*HLA-DQB1*02:01*	14.2	12.6
*HLA-DQB1*02:02*	5.3	9.5
*HLA-DQB1*03:01*	20.5	18.0
*HLA-DQB1*03:02*	10.6	10.2
*HLA-DQB1*03:03*	3.7	4.6
*HLA-DQB1*04:02*	3.9	2.7
*HLA-DQB1*05:01*	14.9	11.9
*HLA-DQB1*05:02*	2.6	1.5
*HLA-DQB1*05:03*	2.1	2.7
*HLA-DQB1*06:02*	12.4	14.8
*HLA-DQB1*06:03*	4.5	6.4
*HLA-DQB1*06:04*	3.7	3.6
*HLA-DPA1*01:03*	80.4	82.1
*HLA-DPA1*02:01*	16.7	14.1
*HLA-DPA1*02:02*	2.6	3.1
*HLA-DPB1*01:01*	6.4	5.4
*HLA-DPB1*02:01*	10.6	12.0
*HLA-DPB1*03:01*	12.4	11.1
*HLA-DPB1*04:01*	41.3	43.8
*HLA-DPB1*04:02*	12.2	12.3
*HLA-DPB1*05:01*	2.0	1.9
*HLA-DPB1*06:01*	2.1	2.1
*HLA-DPB1*10:01*	2.3	1.7
*HLA-DPB1*11:01*	1.1	2.2
*HLA-DPB1*13:01*	4.2	1.7
*HLA-DPB1*14:01*	1.3	1.5
*HLA-DPB1*17:01*	1.0	1.2

Table S6. Scleroderma Prevalence and *HLA-DPB1*13:01* Allele Frequency in Different Populations Around the World.

Population	SSc Prevalence (per million)	SSc Prevalence Reference	*HLA-DPB1*13:01* Allele Frequency (%)	*HLA-DPB1*13:01* Allele Frequency Reference
Buenos Aires, Argentina	296	(32)	2.8	http://www.allelefrequencies.net/pop6001c.asp?pop_id=1310
Tokyo, Japan	38	(33)	1.79	http://www.allelefrequencies.net/pop6001c.asp?pop_id=3279
US-Caucasian	138	(34)	2.4	http://www.allelefrequencies.net/pop6001c.asp?pop_id=2780
UK	88	(35)	2.1	http://www.allelefrequencies.net/pop6001c.asp?pop_id=2511
France	158	(36)	2.73	http://www.allelefrequencies.net/pop6001c.asp?pop_id=2517
US-African American	300	(37)	6	http://www.allelefrequencies.net/pop6001c.asp?pop_id=2779
New Zealand	30	(38)	0.3	http://www.allelefrequencies.net/pop6001c.asp?pop_id=2160
Greece	154	(39)	3	http://www.allelefrequencies.net/pop6001c.asp?pop_id=1759
Choctaw	4690	(40)	22	(41)

Table S7. ***HLA*** **allele associations in autoantibobdy positive and negative subsets in African Americans.**

		Freq % (SSc/Ctrls)	OR (95% CI) UnConditioned	P-value UnConditioned
All SSc v controls SSc=662; Control=946	***HLA-DRB1*0804***	**24.3 / 9.3**	**3.2 (2.4-4.3)**	**3.26×10^{-16}**
	*HLA-DQB1*0319*	18.4 / 8.8	2.4 (1.8-3.2)	2.45×10^{-8}
	*HLA-DQB1*0301*	37 / 25.8	1.8 (1.4-2.2)	1.41×10^{-6}
	*HLA-DRB1*0701*	11.5 / 20	0.6 (0.4-0.7)	2.72×10^{-6}
	*HLA-DQA1*0201*	11.5 / 20	0.6 (0.4-0.7)	3.18×10^{-6}
	HLA-DRB1*1102	**13.6 / 7.1**	**2.2 (1.6-3)**	**9.39×10^{-6}**
	*HLA-DPA1*0201*	62.1 / 51.5	1.6 (1.3-1.9)	3.20×10^{-5}
	*HLA-DPB1*1301*	16.9 / 9.7	1.9 (1.4-2.6)	3.21×10^{-5}
AFA+ SSc v controls SSc=129; Control=946	***HLA-DRB1*0804***	**42.6 / 9.3**	**7.4 (4.9-11.3)**	**2.61×10^{-19}**
	HLA-DQB1*0609	**20.9 / 6.6**	**3.8 (2.3-6.3)**	**1.37×10^{-6}**
	*HLA-DQB1*0301*	45 / 25.8	2.5 (1.7-3.6)	9.16×10^{-6}
	*HLA-DQB1*0319*	22.5 / 8.8	3 (1.9-4.9)	2.53×10^{-5}
	*HLA-DRB1*1302*	29.5 / 13.8	2.6 (1.7-4)	3.70×10^{-5}
AFA- SSc v controls SSc=533; Control=946	*HLA-DRB1*0804*	19.9 / 9.3	2.5 (1.8-3.3)	1.05×10^{-8}
	*HLA-DQB1*0609*	5.6 / 6.6	0.9 (0.6-1.4)	0.62
ATA+ SSc v controls SSc=183; Control=946	***HLA-DPB1*1301***	**30.6 / 9.7**	**4.3 (2.9-6.3)**	**2.35×10^{-12}**
	HLA-DQB1*0201	**7.7 / 25.1**	**0.3 (0.2-0.5)**	**1.10×10^{-8}**
	*HLA-DRB1*0301*	3.3 / 14.9	0.2 (0.1-0.5)	4.92×10^{-7}
	*HLA-DQB1*0301*	43.7 / 25.8	2.3 (1.7-3.1)	2.64×10^{-6}
	*HLA-DPA1*0201*	69.9 / 51.5	2.3 (1.6-3.2)	2.73×10^{-6}
	*HLA-DRB1*0804*	21.3 / 9.3	2.8 (1.8-4.2)	8.13×10^{-6}
	*HLA-DQA1*0501*	51.4 / 39.1	1.6 (1.2-2.2)	2.90×10^{-3}
ATA- SSc v controls SSc=479; Control=946	*HLA-DPB1*1301*	11.7 / 9.7	1.2 (0.9-1.7)	0.27
	*HLA-DQB1*0201*	22.1 / 25.1	0.8 (0.7-1.1)	0.21

** Frequency of individuals with one or two alleles.*
*Common AA haplotype: HLA-DRB1*08:04/DQA1*05:01/DQB1*03:01.*

Table S8. *HLA* allele associations in autoantibobdy positive and negative subsets in European Americans.

		Freq % (SSc/Ctrls)	*OR (95% CI)* UnConditioned	*P-value* UnConditioned
All SSc v controls SSc=723; Control=5437	***HLA-DQB1*0202***	**10.2 / 18**	**0.5 (0.4-0.6)**	**3.55×10^{-9}**
	*HLA-DRB1*0701*	15.1 / 23.7	0.5 (0.4-0.7)	6.06×10^{-9}
	*HLA-DQA1*0201*	15.8 / 24.3	0.6 (0.4-0.7)	1.04×10^{-8}
	HLA-DPB1*1301	**8.3 / 3.3**	**2.6 (1.9-3.5)**	**1.75×10^{-8}**
	HLA-DRB1*1104	**10.5 / 4.7**	**2.2 (1.7-2.9)**	**9.25×10^{-8}**
	*HLA-B*4403*	5.1 / 9.7	0.5 (0.3-0.7)	4.72×10^{-6}
	*HLA-DRB1*0101*	23.7 / 17.3	1.5 (1.2-1.8)	4.39×10^{-5}
ATA+ SSc v controls SSc=115; Control=5437	***HLA-DPB1*1301***	**32.2 / 3.3**	**13.7 (8.9-21)**	**1.47×10^{-24}**
	HLA-DRB1*1104	**25.2 / 4.7**	**6.3 (3.9-10)**	**8.62×10^{-12}**
	*HLA-DPA1*0201*	48.7 / 26.3	2.9 (2-4.2)	8.70×10^{-8}
	*HLA-DPA1*0103*	54.8 / 32.6	2.7 (1.8-3.9)	4.65×10^{-7}
ATA- SSc v controls SSc=608; Control=5437	*HLA-DPB1*1301*	3.8 / 3.3	1.1 (0.7-1.7)	0.65
	*HLA-DRB1*1104*	7.7 / 4.7	1.6 (1.1-2.2)	8.81×10^{-3}
ACA+ SSc v controls SSc=238; Control=5437	***HLA-DRB1*0701***	**3.4 / 23.7**	**0.1 (0.05-0.2)**	**4.79×10^{-20}**
	*HLA-DQA1*0201*	4.6 / 14.5	0.1 (0.1-0.2)	4.85×10^{-18}
	*HLA-DQB1*0202*	2.9 / 18	0.1 (0.1-0.3)	2.44×10^{-14}
	HLA-DQB1*0501	**42.4 / 22.3**	**2.3 (1.8-3)**	**4.21×10^{-9}**
	*HLA-DQA1*0101*	47.5 / 26.7	2.2 (1.7-2.9)	7.08×10^{-9}
	*HLA-DRB1*0101*	34.5 / 17.3	2.2 (1.7-3)	1.32×10^{-7}
	HLA-DQA1*0401	**14.3 / 5.4**	**2.7 (1.8-4)**	**4.18×10^{-6}**
	*HLA-DQB1*0303*	2.1 / 8.9	0.2 (0.1-0.5)	6.29×10^{-6}
	*HLA-DRB1*0801*	11.8 / 4.6	2.6 (1.7-3.9)	4.97×10^{-5}
ACA- SSc v controls SSc=485; Control=5437	*HLA-DRB1*0701*	20.8 / 23.7	0.8 (0.7-1.1)	0.13
	*HLA-DQB1*0501*	19.4 / 22.3	0.9 (0.7-1.1)	0.28
	*HLA-DQA1*0401*	5.2 / 5.4	1.0 (0.6-1.5)	0.95

** Frequency of individuals with one or two alleles.*
*Common EA haplotypes: HLA-DRB1*11:04/DQA1*05:01/DQB1*03:01.*
*Common EA haplotypes: HLA-DRB1*07:01/DQA1*02:01/DQB1*02:02.*

Table S9. Predicted immunodominant peptides in topoisomerase I protein; peptide in red shown in the manuscript in Figure 5.

ATA+ SSc Subset				
Ancestry	**Peptide**		**Affinity (nM)**	
	Position	**Sequence**	***DPA1*02:01/DPB1*13:01***	***DRA1*01:01/DRB1*11:04***
EA	420	IQGSIKYIMLNPSSR	498.1	132.1
	421	QGSIKYIMLNPSSRI	357.6	81.7
	422	GSIKYIMLNPSSRIK	374.8	59.9
	423	SIKYIMLNPSSRIKG	448.4	58.4
	468	KEMKVRQRAVALYFI	492.6	94.0
	469	EMKVRQRAVALYFID	488.2	169.7
	470	MKVRQRAVALYFIDK	397.4	290.8
	473	**RQRAVALYFIDKLAL**	**264.2**	**340.3**
	474	QRAVALYFIDKLALR	320.0	195.9
	475	RAVALYFIDKLALRA	340.4	131.0
	476	AVALYFIDKLALRAG	481.1	117.5
	541	VPVEKRVFKNLQLFM	400.4	391.4
	542	PVEKRVFKNLQLFME	224.8	361.4
	543	VEKRVFKNLQLFMEN	187.4	328.0
	544	EKRVFKNLQLFMENK	187.4	306.2
	545	KRVFKNLQLFMENKQ	246.2	311.3
	546	RVFKNLQLFMENKQP	408.9	456.4
	Position	**Sequence**	***DPA1*02:01/DPB1*13:01***	***DQA1*05:01/DQB1*02:01***
AA	472	VRQRAVALYFIDKLA	268.2	489.2
	473	**RQRAVALYFIDKLAL**	**264.2**	**446.4**

Table S10. Predicted immunodominant peptides in fibrillarin protein; peptide in red shown in the manuscript in Figure 5. ***(LD=linkage disequilibrium)***

Ancestry	Peptide		AFA+ SSc Subset Affinity (nM)		in tight LD
	Position	Sequence	*DRA1*01:01/DRB1*08:04*	*DQA1*01:02/DQB1*06:09*	*DRA1*01:01/DRB1*13:02*
	130	DKIEYRAWNPFRSKL	491.0	15195.4	455.9
	131	KIEYRAWNPFRSKLA	296.5	13720.9	377.2
	132	IEYRAWNPFRSKLAA	276.3	14399.6	539.5
	133	EYRAWNPFRSKLAAA	270.5	14939.3	810.2
	134	YRAWNPFRSKLAAAI	230.8	11841.2	359.9
	135	RAWNPFRSKLAAAIL	235.1	10171.3	226.2
	136	AWNPFRSKLAAAILG	273.8	9922.7	270.4
	137	WNPFRSKLAAAILGG	315.4	9407.5	332.6
	138	NPFRSKLAAAILGGV	381.7	7104.8	390.8
	151	GVDQIHIKPGAKVLY	323.8	19226.5	90.4
	152	VDQIHIKPGAKVLYL	249.2	17250.9	69.1
	153	DQIHIKPGAKVLYLG	270.0	18134.6	86.8
	154	QIHIKPGAKVLYLGA	245.7	16850.1	106.1
	155	IHIKPGAKVLYLGAA	404.1	15835.1	285.2
	184	DGLVYAVEFSHRSGR	465.1	14957.9	1244.2
	185	GLVYAVEFSHRSGRD	435.2	18178.8	1278.0
	186	LVYAVEFSHRSGRDL	466.2	21658.7	1284.4
	194	HRSGRDLINLAKKRT	385.0	22684.5	1421.1
	195	RSGRDLINLAKKRTN	181.6	23578.4	1106.2
	196	SGRDLINLAKKRTNI	108.3	24642.8	689.9
	197	**GRDLINLAKKRTNII**	**81.2**	**24260.5**	**131.0**
AA	198	RDLINLAKKRTNIIP	88.1	24504.6	119.5
	199	DLINLAKKRTNIIPV	116.0	21083.4	83.3
	200	LINLAKKRTNIIPVI	124.4	14049.4	50.2
	201	INLAKKRTNIIPVIE	361.8	12731.9	55.4
	217	ARHPHKYRMLIAMVD	438.2	10118.4	725.3
	218	RHPHKYRMLIAMVDV	342.1	7057.2	520.4
	219	HPHKYRMLIAMVDVI	322.0	3925.2	236.0
	220	PHKYRMLIAMVDVIF	312.9	3051.9	215.8
	221	HKYRMLIAMVDVIFA	258.1	2138.2	167.5
	222	KYRMLIAMVDVIFAD	303.3	2100.7	197.0
	239	QPDQTRIVALNAHTF	485.1	9365.3	53.4
	240	PDQTRIVALNAHTFL	294.7	7407.5	23.5
	241	DQTRIVALNAHTFLR	202.7	7323.3	18.1
	242	QTRIVALNAHTFLRN	169.6	7269.3	17.6
	243	TRIVALNAHTFLRNG	197.6	8079.4	20.3
	244	RIVALNAHTFLRNGG	265.1	9136.4	25.5
	255	RNGGHFVISIKANCI	269.0	8703.3	35.4
	256	NGGHFVISIKANCID	280.2	8921.2	33.4
	257	GGHFVISIKANCIDS	243.7	8594.8	30.1
	258	GHFVISIKANCIDST	268.2	7873.6	28.8
	259	HFVISIKANCIDSTA	370.3	7776.0	31.6
	306	HAVVVGVYRPPPKVK	466.8	20434.6	1590.8

Table S11. (A) Predicted immunodominant peptides in Centromere Protein A; peptide in red shown in the manuscript in Figure 5. ***(LD=linkage disequilibrium)***

ACA+ SSc Subset (CENPA)					in tight LD
Ancestry	Peptide		Affinity (nM)		
	Position	Sequence	*DRA1*01:01/DRB1*07:01*	*DQA1*01:01/DQB1*05:01*	*DRA1*01:01/DRB1*01:01*
EA	48	LKEIRKLQKSTHLLI	93.0	8523.5	68.4
	49	KEIRKLQKSTHLLIR	77.1	7917.4	57.1
	50	EIRKLQKSTHLLIRK	78.0	7992.8	60.5
	51	IRKLQKSTHLLIRKL	68.5	6146.3	56.1
	52	RKLQKSTHLLIRKLP	86.8	6388.9	77.2
	53	KLQKSTHLLIRKLPF	127.2	4942.0	105.9
	54	LQKSTHLLIRKLPFS	237.8	4827.6	142.8
	55	QKSTHLLIRKLPFSR	467.8	5302.3	140.4
	56	KSTHLLIRKLPFSRL	203.0	3881.7	68.2
	57	STHLLIRKLPFSRLA	188.1	3895.0	51.2
	58	THLLIRKLPFSRLAR	181.8	4310.4	44.4
	59	HLLIRKLPFSRLARE	211.8	4498.2	48.6
	60	LLIRKLPFSRLAREI	222.9	4538.8	54.5
	61	LIRKLPFSRLAREIC	321.5	4876.5	85.7
	62	IRKLPFSRLAREICV	378.2	4487.2	124.9
	63	RKLPFSRLAREICVK	456.5	5468.0	141.4
	64	KLPFSRLAREICVKF	391.3	4588.5	121.0
	65	LPFSRLAREICVKFT	459.3	5060.8	134.7
	70	LAREICVKFTRGVDF	181.91	6722.66	430.14
	71	AREICVKFTRGVDFN	143.5	6184.14	330.53
	72	REICVKFTRGVDFNW	115.22	3606.71	259.57
	73	EICVKFTRGVDFNWQ	123.03	3264.66	252.81
	74	ICVKFTRGVDFNWQA	130.89	2920.06	243.49
	75	CVKFTRGVDFNWQAQ	211.61	2645.54	327.23
	76	VKFTRGVDFNWQAQA	416.33	2178.19	448.15
	78	FTRGVDFNWQAQALL	447.63	540.61	187.33
	79	TRGVDFNWQAQALLA	296.61	477.89	78.89
	80	RGVDFNWQAQALLAL	175.7	357.28	48.24
	81	GVDFNWQAQALLALQ	186.48	433.62	42.93
	82	VDFNWQAQALLALQE	225.37	498.32	49.91
	83	DFNWQAQALLALQEA	297.42	657.02	60.8
	84	FNWQAQALLALQEAA	424.77	919.85	72.45
	88	AQALLALQEAAEAFL	499.45	735.43	24.84
	89	QALLALQEAAEAFLV	251.33	718.16	21.3
	90	ALLALQEAAEAFLVH	247.9	907.73	24.72
	91	LLALQEAAEAFLVHL	222.56	972.33	32.62
	92	LALQEAAEAFLVHLF	222.81	604.19	66.65
	93	ALQEAAEAFLVHLFE	326.61	435.3	204.64
	94	**LQEAAEAFLVHLFED**	**445.81**	**304.33**	**299.55**
	97	AAEAFLVHLFEDAYL	477.35	61.41	171.15
	98	AEAFLVHLFEDAYLL	326.8	51.99	106.63
	99	EAFLVHLFEDAYLLT	310.85	52.9	90.65
	100	AFLVHLFEDAYLLTL	267.15	55.82	82.51
	101	FLVHLFEDAYLLTLH	314.62	70.32	95.24
	102	LVHLFEDAYLLTLHA	429.45	115.73	111.14
	104	HLFEDAYLLTLHAGR	404.46	873.56	69.17
	105	LFEDAYLLTLHAGRV	87.65	1214.72	25.75
	106	FEDAYLLTLHAGRVT	68.79	2011.59	18.77
	107	EDAYLLTLHAGRVTL	50.05	2766.4	15.38
	108	DAYLLTLHAGRVTLF	40.32	2062.5	13.95
	109	AYLLTLHAGRVTLFP	42.44	2017.48	14.46
	110	YLLTLHAGRVTLFPK	51.87	2284.67	17.66
	111	LLTLHAGRVTLFPKD	97.22	3118.21	35.61
	112	LTLHAGRVTLFPKDV	318.83	4232.43	148.92

Table S11. (B) Predicted immunodominant peptides in Centromere Protein B *(LD=linkage disequilibrium) (continued on next page).*

			ACA+ SSc Subset (CENPB)		
Ancestry	Peptide		Affinity (nM)		in tight LD
	Position	Sequence	*DRA1*01:01/DRB1*07:01*	*DQA1*01:01/DQB1*05:01*	*DRA1*01:01/DRB1*01:01*
	3	PKRRQLTFREKSRII	375.95	11822.26	353.19
	4	KRRQLTFREKSRIIQ	316.44	11434.78	225.98
	5	RRQLTFREKSRIIQE	352.09	11172.33	218.04
	6	RQLTFREKSRIIQEV	290.65	8483.02	175.26
	7	QLTFREKSRIIQEVE	419.57	7673.62	246.06
	30	EIARRFNIPPSTLST	495.35	3670.44	104.18
	31	IARRFNIPPSTLSTI	313.12	5271.36	62.96
	32	ARRFNIPPSTLSTIL	253.04	8886.34	52.78
	33	RRFNIPPSTLSTILK	294.55	15951.31	62.32
	34	RFNIPPSTLSTILKN	497.14	15988.46	118.19
	39	PSTLSTILKNKRAIL	467.87	13153.38	93.81
	40	STLSTILKNKRAILA	344.35	10784.31	56.92
	41	TLSTILKNKRAILAS	338.26	10203.69	47.51
	42	LSTILKNKRAILASE	393.67	9622.73	50.87
	43	STILKNKRAILASER	444.64	9850.9	57.54
	68	TNKLSPYDKLEGLLI	307.16	4395.45	91.01
	69	NKLSPYDKLEGLLIA	212.84	3614.64	43.45
	70	KLSPYDKLEGLLIAW	193.34	3322.86	34.99
	71	LSPYDKLEGLLIAWF	166.91	2104.14	30.51
	72	SPYDKLEGLLIAWFQ	203.33	1718.01	34.41
	73	PYDKLEGLLIAWFQQ	263.81	1137.75	43.55
	74	YDKLEGLLIAWFQQI	407.91	528.68	74.25
	77	LEGLLIAWFQQIRAA	442.11	211.2	121.31
	78	EGLLIAWFQQIRAAG	434.52	249.2	94.61
	79	GLLIAWFQQIRAAGL	25.94	279.05	12.04
	80	LLIAWFQQIRAAGLP	25.38	373.15	9.69
	81	LIAWFQQIRAAGLPV	19.47	663.45	8.11
	82	IAWFQQIRAAGLPVK	19.03	1687.92	7.39
	83	AWFQQIRAAGLPVKG	22.38	4397.83	7.83
	84	WFQQIRAAGLPVKGI	25.76	5498.38	8.55
	85	FQQIRAAGLPVKGII	47.03	6598.28	12.74
	86	QQIRAAGLPVKGIIL	151.25	8575.58	38.69
	87	QIRAAGLPVKGIILK	212.26	9471.19	61.41
	88	IRAAGLPVKGIILKE	364.96	11466.5	120.22
EA	89	RAAGLPVKGIILKEK	389.85	12931.13	125.73
	93	LPVKGIILKEKALRI	91.31	7369.78	37.98
	94	PVKGIILKEKALRIA	73.42	6923.9	21.76
	95	VKGIILKEKALRIAE	82.33	6914.17	21.17
	96	KGIILKEKALRIAEE	96.42	5246.95	22.59
	97	GIILKEKALRIAEEL	133.48	3609.48	29.39
	98	IILKEKALRIAEELG	197.54	3621.92	44.93
	99	ILKEKALRIAEELGM	397.54	2672.15	121.47
	111	LGMDDFTASNGWLDR	366.99	5049.29	393.27
	112	GMDDFTASNGWLDRF	231.32	3800.53	233.65
	113	MDDFTASNGWLDRFR	205.27	2887.85	180.47
	114	DDFTASNGWLDRFRR	282.66	2939.08	249.32
	115	DFTASNGWLDRFRRR	305.7	2927.53	274.66
	128	RRHGVVSCSGVARAR	488.78	13005.77	127.13
	129	RHGVVSCSGVARARA	465.62	11914.08	105
	133	VSCSGVARARARNAA	494.88	16283.33	92.98
	186	YASQDVFSATETSLW	489.38	5457.13	354.48
	187	ASQDVFSATETSLWY	261.92	5093.95	368.91
	188	SQDVFSATETSLWYD	359.7	5261.22	460
	189	QDVFSATETSLWYDF	279.01	3574.89	410.28
	197	TSLWYDFLPDQAAGL	492.06	206.96	99.15
	198	SLWYDFLPDQAAGLC	426.88	335.29	75.43
	199	LWYDFLPDQAAGLCG	480.42	907.77	72.19
	266	KGGVTTQALAKYLKA	497.63	10583.06	165.87
	267	GGVTTQALAKYLKAL	403.36	7981.26	134.97
	268	GVTTQALAKYLKALD	471.8	4837.88	159.07
	269	VTTQALAKYLKALDT	485.14	3868.99	112.51
	271	TQALAKYLKALDTRM	239.47	2736.25	33.03
	272	QALAKYLKALDTRMA	134.65	2182.63	16.75
	273	ALAKYLKALDTRMAA	105.21	2054.29	11.96
	274	LAKYLKALDTRMAAE	118.34	2361.04	12.03
	275	AKYLKALDTRMAAES	145.1	3183.59	13.11
	276	KYLKALDTRMAAESR	182.77	3584.34	15.46
	277	YLKALDTRMAAESRR	338.52	4806.47	24.49
	280	ALDTRMAAESRRVLL	278.71	10228.89	157.6

Table S11. (B) Predicted immunodominant peptides in Centromere Protein B (continued). ***(LD=linkage disequilibrium)***

			ACA+ SSc Subset (CENPB)		
Ancestry	Peptide		Affinity (nM)		in tight LD
	Position	Sequence	*DRA1*01:01/DRB1*07:01*	*DQA1*01:01/DQB1*05:01*	*DRA1*01:01/DRB1*01:01*
	281	LDTRMAAESRRVLLL	189.26	7053.35	119.67
	282	DTRMAAESRRVLLLA	253.76	6448.37	155.62
	283	TRMAAESRRVLLLAG	271.95	6781.77	162.24
	284	RMAAESRRVLLLAGR	462.1	7047.09	247.82
	286	AAESRRVLLLAGRLA	294.88	4448.08	32.83
	287	AESRRVLLLAGRLAA	224.95	3290.41	21.79
	288	ESRRVLLLAGRLAAQ	219.73	2792.3	19
	289	SRRVLLLAGRLAAQS	220.31	2624.69	17.81
	290	RRVLLLAGRLAAQSL	215.46	2156.01	18.77
	291	RVLLLAGRLAAQSLD	339.9	2577.05	27.83
	303	SLDTSGLRHVQLAFF	360.21	2363.32	304.03
	304	LDTSGLRHVQLAFFP	418.89	2067.42	268.87
	305	DTSGLRHVQLAFFPP	472.25	1953.07	271.5
	306	TSGLRHVQLAFFPPG	484.4	1499.69	221.7
	308	GLRHVQLAFFPPGTV	353.72	971.76	148.15
	309	LRHVQLAFFPPGTVH	347.36	1057.65	125.13
	310	RHVQLAFFPPGTVHP	397	1305.75	140.51
	311	HVQLAFFPPGTVHPL	246.97	1508.04	106.6
	312	VQLAFFPPGTVHPLE	282.31	2011.51	115.43
	313	QLAFFPPGTVHPLER	353.21	4171.78	122.41
	329	VVQQVKGHYRQAMLL	467.92	4876.61	228.62
	330	VQQVKGHYRQAMLLK	467.28	4830.82	194.9
	331	QQVKGHYRQAMLLKA	242.82	4250.51	53.26
	332	QVKGHYRQAMLLKAM	179.93	3845.08	31.66
	333	VKGHYRQAMLLKAMA	167.77	3934.94	23.24
	334	KGHYRQAMLLKAMAA	147.21	3419.21	17.13
	335	GHYRQAMLLKAMAAL	152.47	2837.92	15.35
	336	HYRQAMLLKAMAALE	147.18	2037.68	15.03
	337	YRQAMLLKAMAALEG	153.59	1958.19	13.61
	338	RQAMLLKAMAALEGQ	162.71	2037.84	12.87
	339	QAMLLKAMAALEGQD	224.18	2248.26	14.86
	340	AMLLKAMAALEGQDP	280.36	2439.41	16.68
	341	MLLKAMAALEGQDPS	382.12	2788.16	21.12
	353	DPSGLQLGLTEALHF	75.41	1973.12	61.73
EA	354	PSGLQLGLTEALHFV	45.14	1408.73	38.76
	355	SGLQLGLTEALHFVA	37.17	1262.23	33.01
	356	GLQLGLTEALHFVAA	34.65	1236.62	33.48
	357	LQLGLTEALHFVAAA	40.73	1241.73	44.3
	358	QLGLTEALHFVAAAW	61.12	914.02	66.47
	359	LGLTEALHFVAAAWQ	121.87	875.41	97.8
	360	GLTEALHFVAAAWQA	161.26	838.91	61.96
	361	LTEALHFVAAAWQAV	53.13	683.6	26
	362	TEALHFVAAAWQAVE	52.96	659.3	21.74
	363	EALHFVAAAWQAVEP	57.93	603.24	21.78
	364	ALHFVAAAWQAVEPS	63.45	618.86	22.45
	365	LHFVAAAWQAVEPSD	89.03	826.93	28.39
	366	HFVAAAWQAVEPSDI	114.93	890.53	45.34
	367	FVAAAWQAVEPSDIA	201.46	1046.22	96.05
	368	VAAAWQAVEPSDIAA	256.34	1990.64	138.31
	369	AAAWQAVEPSDIAAC	308.33	3606.79	164.34
	370	AAWQAVEPSDIAACF	380.43	5990.71	204.19
	538	EVPVPSFGEAMAYFA	348.08	3153.32	146.22
	539	VPVPSFGEAMAYFAM	181.1	2399.13	65.53
	540	PVPSFGEAMAYFAMV	125.36	1206.91	46.1
	541	VPSFGEAMAYFAMVK	105.57	883.58	36.01
	542	PSFGEAMAYFAMVKR	119.34	705.1	39.17
	543	SFGEAMAYFAMVKRY	128.18	566.98	44.58
	544	FGEAMAYFAMVKRYL	119.08	535.35	50.39
	545	GEAMAYFAMVKRYLT	97.64	698.09	43.9
	546	EAMAYFAMVKRYLTS	96.14	891.11	36.51
	547	AMAYFAMVKRYLTSF	93.24	1466.01	32.8
	548	MAYFAMVKRYLTSFP	107.41	2142.15	36.81
	549	AYFAMVKRYLTSFPI	46.74	1850.09	28.5
	550	YFAMVKRYLTSFPID	54.2	1556.56	31.19
	551	FAMVKRYLTSFPIDD	69.94	927.84	45.09
	552	AMVKRYLTSFPIDDR	70.67	620.35	39.94
	553	MVKRYLTSFPIDDRV	69.52	424.57	37.95
	554	VKRYLTSFPIDDRVQ	88.71	453.78	46.03
	555	KRYLTSFPIDDRVQS	156.74	524.42	77.53

Table S12. Bioinformatically derived immunodominant peptides and homologous viral protein identification. (A) Peptide sequences from microbial proteins homologous to topoisomerase I immunodominant peptide; (B) Peptide sequences from microbial proteins homologous to fibrillarin immunodominant peptide; and (C) Peptide sequences from microbial proteins homologous to CENPA immunodominant peptide.

A

Topoisomerase I					
Source	**Protein**	**NCBI Accession**	**E-Value**	**% Homology**	**Sequence**
Human	Topoisomerase I	AAL10791	-	100	**R Q R A V A L Y F I D K L A L**
Hokovirus HKV1	DNA topoisomerase IB	ARF10236.1	0.000003	93	R Q I A V A L Y F I D K L A L
Megavirus chiliensis	DNA topoisomerase 1b	YP_004894910.1	0.003	80	R Q I A T A L Y F I D K F A L
Megavirus vitis	DNA topoisomerase 1b	AVL94169.1	0.003	80	R Q I A T A L Y F I D K F A L
Powai lake megavirus	Hypothetical protein	ANB50940.1	0.003	80	R Q I A T A L Y F I D K F A L
Klosneuvirus KNV1	DNA topoisomerase IB	ARF11421.1	0.003	80	R Q I A T A L Y F I D K F A L
Catovirus CTV1	DNA topoisomerase IB	ARF08721.1	0.013	80	R Q I A T A L Y F I D K F A L

B

Fibrillarin					
Source	**Protein**	**NCBI Accession**	**E-Value**	**% Homology**	**Sequence**
Human	Fibrillarin	EAW56925	-	100	**G R D L I N L A K K R T N I I**
Acanthamoeba polyphaga moumouvirus	Cell division cycle 123 protein	YP_007354044.1	0.004	65	D L I N L A K K I-- --N N I I
Saudi moumouvirus	Cell division cycle	AQN67932	0.004	65	D L I N L A K K I-- --N N I I
Moumouvirus Monve	Hypothetical protein mv_R1060	AEX63262	0.004	65	D L I N L A K K I-- --N N I I

C

CENPA					
Source	**Protein**	**NCBI Accession**	**E-Value**	**% Homology**	**Sequence**
Human	Centromere protein A	AAH02703	-	100	**L Q E A A E A F L V H L F E D**
Dishui lake phycodnavirus 1	Hypothetical protein DSLPV1_013	YP_009465730.1	0.01	80	L Q E A A E A Y L T S L F E D

Exact match
Conservative amino acid substitution

Table S13. (A) Fifty 15-mer Random sequence peptides generated using ExPASy compared with viral sequence database for homology.

https://web.expasy.org/randseq/

	Number of Results		Results with E-value <1	
Peptide Sequence	**Viruses with E-value <1**	**Mimiviridae with E-value <10**	**Virus**	**E-Value**
VKFIQNSEALDRGPT	0	0		
EIVTSAPKNQGFLRD	0	0		
SQLPARDTGKEVINF	0	0		
EINSTPGQAVKLFRD	0	0		
TKRLPSNEAFIDGQV	0	0		
FPASGEKRINTLVQD	0	0		
KLGDPNSIATFVERQ	0	0		
SRVPAKDFLQNGIET	0	0		
SITARQEKPNVLFDG	0	0		
VQGRSDLIENTFAPK	0	0		
DKVEQATRFPGSLNI	0	0		
KIGAPEQNVLDTFSR	0	0		
ADLSTFRQKIGNVPE	1	0	Turkeypox virus	0.61
FGLKNTRAPEQVIDS	0	0		
IEFVPSTKQLGARDN	0	0		
IVANEDPSGKFTLRQ	0	0		
KDGLPQEFITRSNAV	0	0		
KNRAVPTQSDELIGF	0	0		
NQDKPRAVESFITLG	0	0		
FLVQIDNAPGKRSET	0	0		
NVISLPKGAETFQRD	0	0		
QRNEIDGATVLPKFS	1	0	Streptomyces phage	0.93
NALDVRISQEKPTFG	0	0		
SQFPITRLENKVDGA	0	0		
FRITNKDGSAPQLVE	0	0		
LTKSVIDGPENFQAR	0	0		
QNFEVRDGLSTKIAP	0	0		
IQVGFNKAEPDLTRS	0	0		
EGNFLTSPRIQADVK	2	0	Hepacivirus F Rodent hepacivirus	0.66
ELANKTFDSPRQGVI	1	0	Hepatitis C virus subtype 1b	0.33
QFSEIPRTVANDLGK	0	0		
AEIPTDLFQGKNSVR	0	0		
TGRKDFEIQPSLVAN	0	0		
PAEINKVTFSDGQLR	0	0		
SGFRALVKITPNEDQ	0	0		
ERNDATFILKGPQVS	0	0		
TNAISQFRGLDKEPV	0	0		
TAVNREQGFISDLKP	0	0		
AVEDGPQFKSLIRNT	0	0		
DQKAGELVTRPFNIS	0	0		
DNEVKIPSTRAQGLF	0	0		
VGPFTLENADKQISR	0	0		
SQVDPTRFLNIGEAK	0	0		
ASGNLPTVQDKIFER	0	0		
QKFAPISLTGERVDN	0	0		
NGFLTVEPIDSRQKA	0	0		
RADITVQSEKFNGLP	0	0		
FLGDETPQNRIVAKS	0	0		
EFKDTGANIQSPRLV	0	0		
TPKQLNEAVRISDGF	1	0	Human immunodeficiency virus 1	0.33

Table S13. (B) Fifty 15-mer Random sequence peptides generated using SMS compared with viral sequence database for homology.

http://www.bioinformatics.org/sms2/random_protein.html

	Number of Results		Results with E-value <1	
Peptide Sequence	**Viruses with E-value <1**	**Mimiviridae with E-value <10**	**Virus**	**E-Value**
EAAWCSQHLDADFTH	0	0		
DKNWFMLKLGKVITG	0	0		
WLHDIDMCEISASMQ	0	0		
RGGGIGDNFCYWTGP	0	0		
DRVLHEWISNTPSVN	1	0	Saimiriine betaherpesvirus 4	0.61
CYIGHGTGKLIRLRC	0	0		
KFERHHDAYLWVYIE	0	0		
ENKTTMNPAATPDPS	0	0		
ICIPQYYMPATSKIQ	2	0	Escherichia phage EcS1 Serratia phage CHI14	0.43
SAACVPSVKVSIMPC	0	0		
DSNSRKVCQYSQCMG	0	0		
EWAWNRDGISHYIAM	1	0	Pithovirus sibericum	0.87
QFSWPDSLGMPTAKS	0	0		
MWKYGHDITGNFSTC	0	0		
AHFVAEIVQSFFPIG	0	0		
RPFKYMGMFHQHWLQ	0	0		
STHDFMATLFCDGSS	0	0		
ENWDSNHCYGRHYQL	0	0		
DSKYMTFLAICANCS	0	0		
CNHCCFWEPKRGLLP	0	0		
ETFGPLNFLANTQEW	0	0		
AMIFCFLRHEASFSP	0	0		
VKFMWHRLAHIFFRA	0	0		
QPDFWKSYPCQPKLQ	0	0		
CISPYFESTGACPTF	1	0	Aphis glycines virus 3	0.33
KDATIVDHVCTVVWQ	0	0		
NIAMDGLAMSLKARR	0	0		
CSDFPHIRGLVILLP	0	0		
RPYKSDHHILCAKNS	0	0		
DHKIKYLSSYYTDPN	0	0		
QNLQQPKCHTEFVDF	0	0		
MTYMDRNNEVNELTK	1	0	Cyanophage S-RIM14	0.93
TKGTWRRGPMARWES	0	0		
PYNKWMSDSDRMTNR	0	0		
TSAHMHCKAGKDALE	0	0		
RWHVMVNWLYIADDG	0	0		
GTEICPMIVYHFIWW	1	0	White spot syndrome virus	0.33
YYTWAQPGKRKCSET	0	0		
WFMWVPAEMQRWHRV	0	0		
CFSQHPNMSRPYMSA	0	0		
IYVEPTIWSARKHLG	0	0		
GGLVTWYAFRDMTDY	0	0		
SPVANHIMPPTFYNG	0	0		
CGGLNELIEWQPPFE	0	0		
CVNQGYVHFLHYQWC	0	0		
GFSPTYSHEENWVAI	0	0		
RCEDPLTILHPAKLC	0	0		
EFPHIMIAHWGAGGM	0	0		
FDSPKELDPTNNDRR	0	0		
ATRNMPPFSRTSCDV	0	0		

Table S14. (A) BLAST results for topoisomerase I immunodominant peptide.

RQRAVALYFIDKLAL in Topoisomerase I		
Protein	**E-Value**	**% Homology**
topoisomerase (DNA) I, isoform CRA_b	0.000000006	100%
Topoisomerase (DNA) I	0.000000006	100%
topoisomerase I	0.000000006	100%
DNA topoisomerase 1	0.000000006	100%
DNA topoisomerase I	0.000000006	100%
DNA topoisomerase I	0.000000006	100%
topoisomerase (DNA) I, isoform CRA_c	0.000000006	100%
DNA topoisomerase I, mitochondrial isoform X1	0.000000006	100%
TOP1MT protein	0.000000006	100%
DNA topoisomerase I, mitochondrial isoform 1 precursor	0.000000006	100%
Topoisomerase (DNA) I, mitochondrial	0.000000006	100%
mitochondrial DNA topoisomerase I	0.000000006	100%
Chain A, Human Dna Topoisomerase I In Covalent Complex With A 22 Base Pair Dna Duplex	0.000000006	100%
Chain A, Human Dna Topoisomerase I (70 Kda) In Complex With The Indolocarbazole Sa315f And Covalent Complex With A 22 Base Pair Dna Duplex	0.000000006	100%
Chain A, Human Topoisomerase I (Topo70) Double Mutant K532rY723F	0.000000006	100%
Chain A, Human Topoisomerase IDNA COMPLEX	0.000000006	100%
Chain A, Human Reconstituted Dna Topoisomerase I In Covalent Complex With A 22 Base Pair Dna Duplex	0.000000006	100%
Chain A, Structural Mechanisms Of Camptothecin Resistance By Mutations In Human Topoisomerase I	0.000000006	100%
Chain C, Structural Mechanisms Of Camptothecin Resistance By Mutations In Human Topoisomerase I	0.000000006	100%
Chain A, Human Dna Topoisomerase I (70 Kda) In Non-Covalent Complex With A 22 Base Pair Dna Duplex Containing An 8-Oxog Lesion	0.000000006	100%
Chain A, Human Topoisomerase I Ara-C Complex	0.000000006	100%
Chain A, Crystal Structure Of Human Topoisomerase I Dna Complex	0.000000006	100%
unnamed protein product	0.000000006	100%
unnamed protein product	0.000000006	100%
DNA topoisomerase I, mitochondrial isoform 2	0.000000006	100%
unnamed protein product	0.000000006	100%
unnamed protein product	0.000000006	100%
topoisomerase (DNA) I, mitochondrial, isoform CRA_e	0.000006	100%
topoisomerase (DNA) I, mitochondrial, isoform CRA_f	0.000006	100%
topoisomerase (DNA) I, mitochondrial, isoform CRA_c	0.000006	100%
topoisomerase (DNA) I, mitochondrial, isoform CRA_a	0.000006	100%
topoisomerase (DNA) I, mitochondrial, isoform CRA_d	0.000006	100%
topoisomerase (DNA) I, mitochondrial, isoform CRA_b	0.000006	100%

Table S14. (B) BLAST results for fibrillarin immunodominant peptide.

GRDLINLAKKRTNII in Fibrillarin		
Protein	**E-Value**	**% Homology**
rRNA 2'-O-methyltransferase fibrillarin	0.000000008	100%
fibrillarin	0.000000008	100%
rRNA 2'-O-methyltransferase fibrillarin isoform X1	0.000000008	100%
FBRL_HUMAN	0.000000008	100%
unnamed protein product	0.000000008	100%
rRNA 2'-O-methyltransferase fibrillarin isoform X2	0.000000008	100%
Unknown (protein for IMAGE:4538098)	0.000000008	100%
Chain A, Human Fibrillarin	0.000000008	100%
FBRL_HUMAN [AA 1- 227]	0.000000008	100%
rRNA/tRNA 2'-O-methyltransferase fibrillarin-like protein 1	0.000001	87%
hCG1641252	0.000001	87%

Table S14. (C) BLAST results for centromere protein A immunodominant peptide.

LQEAAEAFLVHLFED in Centromere Protein A		
Protein	**E-Value**	**% Homology**
Chain A, Cryo-EM structure of CENP-A nucleosome in complex with kinetochore protein CENP-N	0.000000004	100%
Chain A, Structure Of A Cenp-A-Histone H4 Heterodimer In Complex With Chaperone Hjurp	0.000000004	100%
Chain A, The Structure Of The Centromeric Nucleosome Containing Cenp-A	0.000000004	100%
histone H3-like centromeric protein A isoform a	0.000000004	100%
centromere protein A, 17kDa, isoform CRA_b	0.000000004	100%
Chain A, Crystal Structure Of (Cenp-AH4)2 HETEROTETRAMER	0.000000004	100%
Chain A, Complex Structure 6 Of DaxxH3.3(SUB7)H4	0.000001	93%
Chain A, Complex Structure 3 Of DaxxH3.3(SUB5,G90A)H4	0.000001	93%
Chain A, Complex Structure 2 Of DaxxH3.3(SUB5,G90M)H4	0.000001	93%
Chain A, Complex Structure 1 Of DaxxH3.3(SUB5)H4	0.000001	93%
Chain A, Crystal Structure Of Human Nucleosome Containing H3.y	0.000006	80%
histone cluster 2, H3c pseudogene	0.000006	80%
H3L-like histone	0.000008	80%
histone H3-like centromeric protein A isoform b	0.00001	100%
hCG1749005	0.0002	80%
Chain E, Crystal Structure of the heterotypic nucleosome containing human CENP-A and H3.3	0.0002	80%
Chain A, The Crystal Structure Of The Nucleosome Containing H3.6	0.0002	80%
Chain A, The Nucleosome Structure Containing H2b-k120 And H4-k31 Monoubiquitinations	0.0002	80%
Chain A, The Human Nucleosome Structure Containing The Histone Variant H3.3	0.0002	80%
Chain A, The Human Nucleosome Structure Containing The Histone Variant H3.2	0.0002	80%
histone H3.3	0.0002	80%
Chain A, Crystal Structure Of The Nucleosome Containing Histone H3 With The Crotonylated Lysine 122	0.0002	80%
unnamed protein product	0.0002	80%
histone H3.2	0.0002	80%
unnamed protein product	0.0002	80%
H3 histone, family 3A	0.0002	80%
Chain A, Crystal structure of EBV tegument protein BNRF1 in complex with histone chaperone DAXX and histones H3.3-H4	0.0002	80%
Chain M, CryoEM Structure INO80core Nucleosome complex	0.0002	80%
hCG1639761	0.0002	80%
Chain A, Crystal Structure Of Human Mcm2 Hbd And Asf1b Chaperoning A Histone H3.2-h4 Dimer	0.0002	80%
Chain A, Crystal structure of Human MCM2 HBD chaperoning a histone H3-H4 tetramer	0.0002	80%
Chain A, Crystal Structure Of Human Nucleosome Core Particle Containing H3k122q Mutation	0.001	80%
Chain A, Crystal Structure Of Human Nucleosome Core Particle Containing H3k115q Mutation	0.001	80%
Chain A, Crystal Structure Of Human Nucleosome Core Particle Containing H3k79q Mutation	0.001	80%
Chain A, Crystal Structure Of Human Nucleosome Core Particle Containing H3k64q Mutation	0.001	80%
Chain A, Crystal Structure Of Human Nucleosome Core Particle Containing H3k56q Mutation	0.001	80%
Chain A, The Human Nucleosome Structure	0.001	80%
Histone cluster 1, H3i	0.001	80%
histone H3.1	0.001	80%
Histone cluster 1, H3i	0.001	80%
histone H3	0.001	80%
Chain A, Crystal Structure Of The Nucleosome Core Particle	0.001	80%
Chain A, Crystal Structure Of Human Nucleosome Core Particle Lacking H3.1 N- Terminal Region	0.001	80%
Chain G, Crystal Structure Of Human Spt16 Mid-aid/h3-h4 Tetramer Fact Histone Complex	0.001	80%
histone cluster 2 H3 pseudogene 2	0.002	80%
Chain A, The Nucleosome Containing A Testis-Specific Histone Variant, Human H3t	0.012	73%
Chain A, The Nucleosome Containing Human H3.5	0.012	73%
histone H3.1t	0.012	73%
Histone H3-like	0.012	73%
histone H3.3C	0.012	73%
hCG1789848	0.048	71%

Table S15. Predicted immunodominant peptides in other ancestries for (A) topoisomerase I and (B) centromere protein A.

A

ATA+ SSc Subset				
Ancestry	Peptide			Affinity(nM)
	Position	Sequence	Core	*DRA1*01:01/DRB1*15:02*
Japanese Thai	473	RQRAVALYFIDKLAL	VALYFIDKL	299.7
	Position	Sequence	Core	*DPA1*02:01/DPB1*13:01*
Turkish Iranian	473	RQRAVALYFIDKLAL	VALYFIDKL	264.2
	Position	Sequence	Core	*DRA1*01:01/DRB1*11:04*
Turkish Iranian	473	RQRAVALYFIDKLAL	VALYFIDKL	340.3
	Position	Sequence	Core	*DRA1*01:01/DRB1*08:02*
Mexican	473	RQRAVALYFIDKLAL	VALYFIDKL	600.1
	Position	Sequence	Core	*DRA1*01:01/DRB1*16:02*
Choctaw Indian	473	RQRAVALYFIDKLAL	VALYFIDKL	268.8

B

ACA+ SSc Subset				
Ancestry	Peptide			Affinity(nM)
	Position	Sequence	Core	*DQA1*01:01/DQB1*05:01*
Japanese Chinese	94	LQEAAEAFLVHLFED	AEAFLVHLF	304.3
	Position	Sequence	Core	*DQA1*03:03/DQB1*03:01*@
Japanese	94	LQEAAEAFLVHLFED	AEAFLVHLF	400.3
	Position	Sequence	Core	*DQA1*05:03/DQB1*03:01*@
Japanese	94	LQEAAEAFLVHLFED	AEAFLVHLF	421.7
	Position	Sequence	Core	*DQA1*06:01/DQB1*03:01*@
Japanese	94	LQEAAEAFLVHLFED	AEAFLVHLF	578.6

@ Three different haplotypes

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