

**Supplementary Table 1.** Summary of the datasets included in the study

	GWAS Study	Genotyping platform (case / control)	N (case / control) - After genotyping QC steps	N <sub>FINAL</sub> (case / control)	No. variants after imputation and QC	Reference for case/control data (PMID)
<b>Previous SSc GWAS cohorts</b>	Spain 1	Illumina HumanCNV370K / Illumina HumanCNV370K	376/388	361/355	8,274	20383147 / 20383147
	Germany 1	Illumina HumanCNV370K / Illumina HumanHap550k	280/667	257/659	8,039	20383147 / 20383147
	The Netherlands 1	Illumina HumanCNV370K/ Illumina HumanHap550k	201/638	183/626	8,019	20383147 / 20383147
	USA 1	Illumina HumanHap550K / Breast cancer controls CGEMS; prostate cancer controls CGEMS; Illumina iControlDB database	1,491/3,485	1,365/3,219	8,105	20383147 / 20383147
	France	Illumina Human610-Quad BeadChip	564/488	541/470	8,143	21750679 / 21750679
<b>New SSc GWAS cohorts</b>	Spain 2	Illumina HumanCore; HumanCytoSNP-12v2 / Illumina HumanCore	1,293/1,324	1,169/1,262	8,277	31672989 / 28041642
	Germany 2	Illumina HumanCore / Illumina HumanOmniExpressExome 8v1.2.	404/1,149	364/1,133	8,056	31672989 / 28973304
	The Netherlands 2	Illumina HumanCore / Illumina HumanHap550k	541/846	449/812	8,000	31672989 / 20190752
	USA 2	Illumina HumanCore / HumanHap300v1.1	1,430/1,580	1,286/1,388	8,112	31672989 / 18204446
	Italy	Illumina HumanCore / Illumina HumanHap550k	1,018/960	998/952	8,282	31672989 / 26502338; 20190752
	UK	Illumina HumanCore / Affymetrix GeneChip 500K Mapping Array	1,162/2,978	1,094/2,936	8,006	31672989 / 17554300
	Sweden	Illumina HumanCore / Illumina HumanHap300k	192/1,079	170/1,029	8,001	31672989 / 20453842
	Norway	Illumina HumanCore / Illumina HumanHap550K	102/121	96/118	7,769	31672989 / 23055271
	Australia/UK	Illumina OmniExpress / Affymetrix v6	792/2,630	762/2,625	8,005	31672989 / WTCCC2
	<b>META-ANALYSIS</b>			<b>9,846/18,333</b>	<b>9,095/17,584</b>	<b>8,338<sup>1</sup></b>

CGEMS, Cancer Genetic Markers of Susceptibility studies; QC, quality control; SSc, systemic sclerosis.

<sup>1</sup>Total number of variants included in the meta-analysis.

Supplementary Table 2. Linkage disequilibrium assessment ( $r^2$ ) among the independently associated variants in the global analysis.

	HLA_B_0801	rs2844532	rs3094228	rs9268515	AA_DRB1_1le67	AA_DRB1_Tyr60	AA_DRB1_Ala58	HLA_DRB1_1104	HLA_DRB1_1301	rs482044	HLA_DQA1_0401	AA_DQA1_Thr69	rs1142338*	rs1048372*	HLA_DQB1_0202	HLA_DQB1_0501	rs17500468	rs126511*	AA_DPBI_Lcu11	AA_DPBI_1le76	HLA_DPBI_0301	HLA_DPBI_0601	HLA_DPBI_1301	rs9469378	
HLA_B_0801	1.000																								
rs2844532	0.033	1.000																							
rs3094228	0.468	0.011	1.000																						
rs9268515	0.010	0.004	0.007	1.000																					
AA_DRB1_1le67	0.045	0.007	0.050	0.073	1.000																				
AA_DRB1_Tyr60	0.017	0.020	0.023	0.029	0.125	1.000																			
AA_DRB1_Ala58	0.016	0.000	0.011	0.001	0.060	0.023	1.000																		
HLA_DRB1_1104	0.008	0.003	0.050	0.010	0.027	0.008	0.382	1.000																	
HLA_DRB1_1301	0.002	0.001	0.004	0.003	0.087	0.013	0.008	0.003	1.000																
rs482044	0.040	0.031	0.053	0.210	0.029	0.192	0.082	0.030	0.088	1.000															
HLA_DQA1_0401	0.002	0.002	0.003	0.007	0.022	0.009	0.003	0.001	0.002	0.025	1.000														
AA_DQA1_Thr69	0.002	0.002	0.003	0.007	0.018	0.009	0.003	0.001	0.003	0.027	0.929	1.000													
rs1142338*	0.002	0.002	0.003	0.007	0.022	0.009	0.003	0.001	0.002	0.025	1.000	0.929	1.000												
rs1048372*	0.034	0.006	0.044	0.058	0.699	0.094	0.062	0.022	0.098	0.020	0.019	0.021	0.019	1.000											
HLA_DQB1_0202	0.009	0.063	0.015	0.016	0.143	0.455	0.011	0.003	0.005	0.149	0.004	0.005	0.004	0.168	1.000										
HLA_DQB1_0501	0.010	0.005	0.018	0.024	0.069	0.029	0.019	0.008	0.010	0.054	0.005	0.006	0.005	0.089	0.014	1.000									
rs17500468	0.013	0.004	0.000	0.000	0.049	0.023	0.126	0.107	0.000	0.035	0.002	0.002	0.041	0.013	0.073	1.000									
rs1126511*	0.004	0.003	0.003	0.000	0.001	0.011	0.003	0.002	0.000	0.013	0.002	0.002	0.003	0.017	0.000	0.001	1.000								
AA_DPBI_Lcu11	0.004	0.003	0.003	0.000	0.001	0.011	0.003	0.002	0.000	0.013	0.002	0.002	0.003	0.017	0.000	0.001	1.000	1.000							
AA_DPBI_1le76	0.002	0.001	0.000	0.000	0.007	0.004	0.000	0.000	0.002	0.003	0.000	0.000	0.000	0.006	0.000	0.002	0.065	0.065	1.000						
HLA_DPBI_0301	0.000	0.000	0.000	0.000	0.001	0.002	0.002	0.001	0.000	0.000	0.009	0.009	0.000	0.000	0.001	0.000	0.001	0.405	0.405	0.003	1.000				
HLA_DPBI_0601	0.001	0.000	0.000	0.028	0.006	0.002	0.002	0.001	0.001	0.010	0.000	0.000	0.000	0.006	0.001	0.000	0.002	0.063	0.063	0.000	0.002	1.000			
HLA_DPBI_1301	0.002	0.000	0.000	0.002	0.005	0.006	0.000	0.000	0.000	0.001	0.000	0.000	0.003	0.000	0.000	0.001	0.089	0.089	0.816	0.003	0.000	1.000			
rs9469378	0.002	0.000	0.000	0.003	0.010	0.001	0.000	0.000	0.001	0.000	0.001	0.001	0.001	0.008	0.001	0.001	0.011	0.011	0.220	0.004	0.000	0.274	1.000		

In boldface the variants without other variants in LD; AA: amino acids

\*Coding single nucleotide polymorphisms

The image shows a large, dense table with multiple columns and rows. The text within the table is extremely small and difficult to read, appearing as a grid of lines and characters. It likely contains a list of references or a detailed data table, but the individual entries are not discernible.

**Supplementary Table 4.** Number of patients with clinical and serological information included in the study.

<b>GWAS Study</b>	<b>lcSSc (%)</b>	<b>dcSSc (%)</b>	<b>ACA+ (%)</b>	<b>ATA+ (%)</b>	<b>ARA+ (%)</b>	<b>Total Cases</b>
<b>Spain 1</b>	220 (60.94)	90 (24.93)	170 (47.09)	80 (22.16)	NA	361
<b>Germany 1</b>	148 (57.58)	100 (38.91)	116 (45.13)	76 (29.57)	NA	257
<b>Netherlands 1</b>	125 (68.30)	40 (21.85)	42 (22.95)	42 (22.95)	NA	183
<b>USA 1</b>	822 (60.21)	466 (34.13)	395 (28.93)	210 (15.38)	NA	1365
<b>France</b>	341 (63.03)	177 (32.71)	191 (35.30)	123 (22.73)	NA	541
<b>Spain 2</b>	684 (58.51)	282 (24.12)	470 (40.20)	221 (18.90)	25 (2.13)	1169
<b>Germany 2</b>	180 (49.45)	120 (32.96)	133 (36.53)	95 (26.09)	NA	364
<b>Netherlands 2</b>	296 (65.92)	95 (21.15)	143 (31.84)	74 (16.48)	NA	449
<b>USA 2</b>	750 (58.32)	471 (36.62)	411 (31.95)	193 (15.00)	218 (16.95)	1286
<b>Italy</b>	588 (58.91)	193 (19.33)	436 (43.68)	328 (32.86)	197 (19.73)	998
<b>UK</b>	774 (70.74)	236 (21.57)	396 (36.19)	173 (15.81)	118 (10.78)	1094
<b>Sweden</b>	120 (70.58)	50 (29.41)	44 (25.88)	25 (14.70)	NA	170
<b>Norway</b>	59 (61.45)	31 (32.29)	49 (51.04)	15 (15.62)	NA	96
<b>Australia/UK</b>	579 (75.98)	173 (22.70)	348 (45.66)	94 (12.33)	NA	762
<b>Total</b>	5,686 (62.52)	2,524 (27.75)	3,344 (36.77)	1,749 (19.20)	558 (6.14)	9,095

**Supplementary Table 5.** Sequential conditional analysis results with limited cutaneous systemic sclerosis.

<b>Gene</b>	<b>Alleles</b>	<b>Meta p-value<sup>a</sup></b>	<b>OR</b>	<b>Conditioned p-value</b>
<i>HLA-DQA1</i>	<b>DQA1*02:01</b>	5.23E-51	0.54	--
<i>HLA-DRB1</i>	DRB1*08:01	2.74E-33	2.18	8.07E-29
<i>HLA-DRB1</i>	DRB1*11:04	2.69E-26	1.81	5.02E-24
<i>HLA-DQB1</i>	DQB1*05:01	1.07E-21	1.38	7.34E-21
<i>HLA-DPB1</i>	DPB1*13:01	5.46E-14	1.73	2.18E-17
<i>HLA-DRB1</i>	DRB1*13:01	1.94E-11	0.69	1.85E-09

In boldface the alleles exclusively associated with this clinical phenotype, OR: Odds ratio

<sup>a</sup>Comparisons were performed with the control group

**Supplementary Table 6.** Sequential conditional analysis results with diffuse cutaneous systemic sclerosis.

Gene	Alleles	Meta p-value <sup>a</sup>	OR	Conditioned p-value
<i>HLA-DRB1</i>	DRB1*11:04	3.32E-75	3.18	--
<i>HLA-DPB1</i>	DPB1*13:01	2.94E-44	3.12	3.82E-41
<i>HLA-DQA1</i>	<b>DQA1*05:01</b>	1.16E-30	1.49	1.59E-11

In Boldface the alleles exclusively associated with this clinical phenotype, OR: Odds ratio

<sup>a</sup>Comparisons were performed with the control group

**Supplementary Table 7.** Sequential conditional analysis results with anticomere positive patients

Gene	Alleles	Meta p-value <sup>a</sup>	OR	Conditioned p-value
<i>HLA-DQB1</i>	DQB1*05:01	1.16E-66	1.97	--
<i>HLA-DRB1</i>	<b>DRB1*08:01</b>	9.73E-57	3.18	4.00E-64
<i>HLA-DRB1</i>	<b>DRB1*07:01</b>	1.17E-63	0.36	1.84E-45
<i>HLA-DQA1</i>	DQA1*03:01	2.01E-13	1.31	1.97E-20

In Boldface the alleles exclusively associated with this serological phenotype, OR: Odds ratio

<sup>a</sup>Comparisons were performed with the control group

**Supplementary Table 8.** Sequential conditional analysis results with antitopoisomerase positive patients

Gene	Alleles	Meta p-value <sup>a</sup>	OR	Conditioned p-value
<i>HLA-DPB1</i>	DPB1*1301	2.24E-138	6.81	--
<i>HLA-DRB1</i>	DRB1*1104	3.25E-135	4.92	4.57E-127
<i>HLA-DRB1</i>	DRB1*1501	1.76E-15	1.53	3.37E-22
<i>HLA-DPA1</i>	<b>DPA1*0201</b>	7.91E-43	1.87	2.93E-19
<i>HLA-DQB1</i>	<b>DQB1*0301</b>	7.11E-47	1.86	7.00E-19
<i>HLA-DQB1</i>	DQB1*0303	5.67E-11	1.69	4.85E-09

In Boldface the alleles exclusively associated with this serological phenotype, OR: Odds ratio

<sup>a</sup>Comparisons were performed with the control group



**Supplementary Table 9.** Sequential conditional analysis results with anti-RNAPolIII positive patients

<b>Gene</b>	<b>Alleles</b>	<b>Meta p-value<sup>a</sup></b>	<b>OR</b>	<b>Conditioned p-value</b>
HLA-DRB1	DRB1*11:04	1.72E-16	2.64	--

OR: Odds ratio

<sup>a</sup>Comparisons were performed with the control group

**Supplementary Table 10.** Association *p*- values of classical alleles among the different comparisons.

A. Clinical Subtypes				
Alleles	Global analysis	lcSSc vs. Controls	dcSSc vs. Controls	dcSSc vs. lcSSc <sup>a</sup>
DQA1*02:01	1.69E-47	<b>5.23E-51</b>	1.15E-07	2.08E-08
DQA1*05:01	5.50E-22	2.06E-07	<b>1.16E-30</b>	1.76E-11
B. Serological Subtypes				
Alleles	Global analysis	ACA vs. Controls	ATA vs. Controls	ATA vs. ACA <sup>a</sup>
DRB1*08:01	3.06E-28	<b>9.73E-57</b>	0.0013	1.42E-10
DRB1*07:01	1.83E-47	<b>1.17E-63</b>	0.027	3.85E-27
DPA1*02:01	3.77E-07	1.38E-05	<b>2.93E-19</b>	1.09E-40
DQB1*03:01	1.72E-14	1.99E-04	<b>7.11E-47</b>	1.73E-22

In Boldface the significant *p*- values exclusively associated with this serological phenotype

<sup>a</sup>Significant intra-cases comparisons confirm the private association of the classical alleles