### 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_{NOVA} (case / control) | No. variants after imputation and QC | Reference for case/control data (PMID) |
|---------------------|------------------------------------------------------------------------------------------------------|-----------------------------------------------|---------------------------|--------------------------------------|---------------------------------------|
| **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                   |
| **Spain 2**         | Illumina HumanCore; HumanCytoSNP-12v2 / Illumina HumanCore                                         | 1,293/1,324                                  | 1,169/1,262               | 8,277                                | 31672989 / 28041842                   |
| **Germany 2**       | Illumina HumanCore / Illumina HumanOmnisExpressExome 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 / HumanHap500v1.1                                                             | 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                   |
| **UK**              | Illumina HumanCore / Affymetrix GenChip 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 / 20435842                   |
| **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                     |

**META-ANALYSIS**

9,846/18,333  9,095/17,584  8,318

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

1Total number of variants included in the meta-analysis.
Table 2: Linkage disequilibrium assessment (\( r^2 \)) among the independently associated variants in the global analysis.

| Genotype          | \( r^2 \)  | \( p \)   | Genotype          | \( r^2 \)  | \( p \)   | Genotype          | \( r^2 \)  | \( p \)   |
|-------------------|------------|----------|-------------------|------------|----------|-------------------|------------|----------|
| rs482044          | 0.034      | 0.006    | rs17500468        | 0.003      | 0.003    |
| rs1048372         | 0.033      | 0.004    | rs9469378         | 0.001      | 0.002    |
| rs2844532         | 0.022      | 0.034    | rs1126511         | 0.001      | 0.003    |
| rs1126511         | 0.003      | 0.003    | rs1126511         | 0.001      | 0.003    |
| rs1126511         | 0.001      | 0.001    | rs1126511         | 0.001      | 0.003    |

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| Gene Symbol | chr | Position | Expression |
|-------------|-----|----------|------------|
| RNF39       | chr6| 31082285|            |
| ZFP57       | chr6| 31082285|            |
| XXbac-BPG13B8.10 | chr6 | 33082308 |            |
| GABBR1      | chr6| 31079994|            |
| DDX39BP2    | chr6| 30769726|            |
| PAIP1P1     | chr6| 31125257|            |
| XXbac-BPG249D20.9 | chr6 | 31378510 |            |
| PPP1R18     | chr6| 31097971|            |
| TRIM26BP    | chr6| 31242762|            |
| LY6G5C      | chr6| 31106268|            |
| MUC21       | chr6| 31053257|            |
| TNXB        | chr6| 31348580|            |
| PHF1        | chr6| 32671103|            |
Supplementary Table 4. Number of patients with clinical and serological information included in the study.

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

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

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

*Comparisons were performed with the control group


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

| Gene    | Alleles    | Meta p-value$^a$ | OR  | Conditioned p-value |
|---------|------------|------------------|-----|---------------------|
| HLA-DRB1| DRB1*11:04 | 3.32E-75         | 3.18 | --                  |
| HLA-DPB1| DPB1*13:01 | 2.94E-44         | 3.12 | 3.82E-41            |
| HLA-DQA1| DQA1*05:01 | 1.16E-30         | 1.49 | 1.59E-11            |

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

$^a$Comparisons were performed with the control group
| Gene   | Alleles      | Meta p-value | OR  | Conditioned p-value |
|--------|--------------|--------------|-----|---------------------|
| HLA-DQB1 | DQB1*05:01  | 1.16E-66     | 1.97|                     |
| HLA-DRB1 | DRB1*08:01  | 9.73E-57     | 3.18| 4.00E-64            |
| HLA-DRB1 | DRB1*07:01  | 1.17E-63     | 0.36| 1.84E-45            |
| HLA-DQA1 | DQA1*03:01  | 2.01E-13     | 1.31| 1.97E-20            |

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

*Comparisons were performed with the control group.
### Supplementary Table 8. Sequential conditional analysis results with antitopoisomerase positive patients

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

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

*aComparisons were performed with the control group*
**Supplementary Table 9.** Sequential conditional analysis results with anti-RNApolIII positive patients

| Gene      | Alleles  | Meta p-value$^a$ | OR       | Conditioned p-value |
|-----------|----------|------------------|----------|---------------------|
| HLA-DRB1  | DRB1*11:04 | 1.72E-16         | 2.64     | --                  |

OR: Odds ratio

$^a$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* |
|----------|-----------------|--------------------|-------------------|------------------|
| DQA1*02:01 | 1.69E-47 | **5.23E-51** | 1.15E-07 | 2.08E-08 |
| DQA1*05:01 | 5.50E-22 | 2.06E-07 | **1.16E-30** | 1.76E-11 |

### B. Serological Subtypes

| Alleles  | Global analysis | ACA vs. Controls | ATA vs. Controls | ATA vs. ACA* |
|----------|-----------------|------------------|-----------------|-------------|
| DRB1*08:01 | 3.06E-28 | **9.73E-57** | 0.0013 | 1.42E-10 |
| DRB1*07:01 | 1.83E-47 | **1.17E-63** | 0.027 | 3.85E-27 |
| DPA1*02:01 | 3.77E-07 | 1.38E-05 | **2.93E-19** | 1.09E-40 |
| DQB1*03:01 | 1.72E-14 | 1.99E-04 | **7.11E-47** | 1.73E-22 |

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

*Significant intra-cases comparisons confirm the private association of the classical alleles.