

ONLINE SUPPLEMENTARY DATA

Supplementary Table 1. Genotyping platforms used in each of the six cohorts analyzed.

	CASES		CONTROLS	
	ImmunoChip	TaqMan®	ImmunoChip	TaqMan®
Spain	309	1,184	1,517	1,625
Germany	ND	710	ND	376
The Netherlands	ND	364	1,173	601
Italy	256	460	1,270	773
The United Kingdom	258	752	8,610	372
Norway	ND	99	ND	274
TOTAL (N)	823	3,569	12,570	4,021

Cases, data from samples of systemic sclerosis patients; Controls, data from samples of unaffected controls; ND, No data.

Supplementary Table 2. Results of the statistical analyses of systemic sclerosis patients, systemic sclerosis phenotypic and serological subgroups, and unaffected controls for *MIF* rs755622 polymorphism in six European cohorts separately.

Population	Subgroup (N)	MAF (%)	<i>P</i> -value*	SE	OR [CI 95%]**
Spain	Controls (n=3,142)	14.50			
	SSc (n=1494)	16.06	4.83E-2	0.06137	1.13 [1.00-1.27]
	lcSSc (n=1048)	15.22	0.42	0.07058	1.06 [0.92-1.22]
	dcSSc (n=445)	17.87	8.30E-3	0.09456	1.28 [1.07-1.54]
	ACA+ (n=703)	14.58	0.94	0.08363	1.01 [0.85-1.19]
	ATA+ (n=333)	17.72	2.61E-2	0.1076	1.27 [1.03-1.57]
	PF+ (n=322)	18.48	6.84E-3	0.1077	1.34 [1.08-1.65]
	PAH+ (n=104)	19.71	3.65E-2	0.1779	1.45 [1.02-2.05]
Germany	Controls (n=376)	16.22			
	SSc (n=710)	17.82	0.35	0.1208	1.12 [0.88-1.42]
	lcSSc (n=408)	16.67	0.81	0.1364	1.03 [0.79-1.35]
	dcSSc (n=302)	19.37	0.13	0.1428	1.24 [0.94-1.64]
	ACA+ (n=283)	18.02	0.39	0.1475	1.14 [0.85-1.52]
	ATA+ (n=205)	17.07	0.71	0.1643	1.06 [0.77-1.47]
	PF+ (n=215)	16.74	0.82	0.1627	1.04 [0.76-1.43]
	PAH+ (n=33)	18.18	0.68	0.3341	1.15 [0.60-2.21]
The Netherlands	Controls (n=1774)	18.46			
	SSc (n=364)	21.29	0.08	0.1003	1.20 [0.98-1.45]
	lcSSc (n=251)	20.72	0.23	0.1183	1.15 [0.92-1.46]
	dcSSc (n=113)	22.57	0.12	0.1643	1.29 [0.93-1.78]
	ACA+ (n=89)	21.91	0.25	0.1863	1.24 [0.86-1.79]
	ATA+ (n=97)	22.16	0.20	0.1782	1.26 [0.89-1.78]
	PF+ (n=134)	19.03	0.82	0.1615	1.04 [0.76-1.43]
	PAH+ (n=15)	23.33	0.49	0.4338	1.34 [0.57-3.14]
Italy	Controls (n=2043)	13.26			
	SSc (n=716)	13.41	0.89	0.09023	1.01 [0.85-1.21]
	lcSSc (n=534)	13.48	0.85	0.1008	1.02 [0.84-1.24]
	dcSSc (n=182)	13.19	0.97	0.1616	0.99 [0.72-1.36]
	ACA+ (n=297)	12.46	0.59	0.1325	0.93 [0.72-1.21]
	ATA+ (n=252)	13.89	0.70	0.1368	1.06 [0.81-1.38]
	PF+ (n=259)	11.20	0.19	0.1468	0.82 [0.62-1.10]
	PAH+ (n=29)	15.52	0.62	0.3656	1.20 [0.59-2.46]
The United Kingdom	Controls (n=8982)	16.53			
	SSc (n=1010)	15.45	0.21	0.06476	0.92 [0.81-1.05]
	lcSSc (n=750)	15.80	0.46	0.07358	0.95 [0.82-1.09]
	dcSSc (n=260)	14.42	0.20	0.1264	0.85 [0.66-1.09]
	ACA+ (n=388)	17.01	0.73	0.09763	1.04 [0.85-1.25]
	ATA+ (n=179)	15.08	0.47	0.149	0.90 [0.67-1.20]
	PF+ (n=309)	16.18	0.82	0.111	0.97 [0.78-1.21]
	PAH+ (n=40)	18.75	0.59	0.2871	1.17 [0.66-2.05]
Norway	Controls (n=274)	15.88			
	SSc (n=99)	21.21	0.09	0.2095	1.43 [0.95-2.15]
	lcSSc (n=68)	23.53	3.51E-2	0.2335	1.63 [1.03-2.58]
	dcSSc (n=31)	16.13	0.96	0.3645	1.02 [0.50-2.08]
	ACA+ (n=54)	24.07	3.92E-2	0.2536	1.68 [1.02-2.76]
	ATA+ (n=13)	19.23	0.65	0.5112	1.26 [0.46-3.44]
	PF+ (n=35)	20.00	0.38	0.3209	1.33 [0.71-2.48]
	PAH+ (n=9)	22.22	0.47	0.5789	1.51 [0.49-4.71]

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*Unaffected controls are used as reference for the global set of the disease and for each phenotype comparison. **Odds ratio (OR) for the minor allele. MAF, minor allele frequency; CI, confidence interval; SSc, systemic sclerosis; lcSSc, limited cutaneous systemic sclerosis; dcSSc, diffuse cutaneous systemic sclerosis; ACA+, patients with anti-centromere antibodies; ATA+, patients with anti-topoisomerase antibodies; PF+, patients affected by pulmonary fibrosis; PAH+, patients affected by pulmonary arterial hypertension.

Supplementary Table 3. Results of the statistical analyses of four subgroups of patients based on systemic sclerosis-subtype and pulmonary arterial hypertension status and unaffected controls for *MIF* rs755622 in six European cohorts separately.

Population	Subgroup (N)	MAF (%)	P-value*	SE	OR [CI 95%]**
Spain	Controls (n=3,142)	14.50			
	dcSSc with PAH (n=18)	25.00	0.07	0.3866	1.97 [0.92-4.19]
	lcSSc with PAH (n=86)	18.60	0.13	0.1992	1.35 [0.91-1.99]
	dcSSc without PAH (n=329)	17.93	1.83E-2	0.1078	1.29 [1.04-1.59]
	lcSSc without PAH (n=753)	14.50	0.62	0.08056	1.04 [0.89-1.22]
Germany	Controls (n=376)	16.22			
	dcSSc with PAH (n=10)	25.00	0.30	0.5258	1.72 [0.61-4.82]
	lcSSc with PAH (n=23)	15.22	0.86	0.4222	0.93 [0.41-2.12]
	dcSSc without PAH (n=221)	20.36	0.07	0.1541	1.32 [0.98-1.79]
	lcSSc without PAH (n=270)	17.04	0.70	0.1513	1.06 [0.79-1.43]
The Netherlands	Controls (n=1,774)	18.46			
	dcSSc with PAH (n=2)	75.00	3.63E-3	1.156	13.25 [1.38-127.6]
	lcSSc with PAH (n=13)	15.38	0.69	0.5453	0.80 [0.23-2.34]
	dcSSc without PAH (n=58)	19.83	0.71	0.2369	1.09 [0.69-1.74]
	lcSSc without PAH (n=173)	20.23	0.42	0.1406	1.12 [0.85-1.48]
Italy	Controls (n=2,043)	13.26			
	dcSSc with PAH (n=2)	0	0.43	Inf	NA
	lcSSc with PAH (n=27)	16.67	0.46	0.368	1.31 [0.64-2.69]
	dcSSc without PAH (n=149)	13.09	0.93	0.1778	0.98 [0.69-1.40]
	lcSSc without PAH (n=412)	13.59	0.80	0.1116	1.03 [0.83-1.28]
The United Kingdom	Controls (n=8982)	16.53			
	dcSSc with PAH (n=2)	50.00	0.07	1	5.05 [0.71-35.86]
	lcSSc with PAH (n=38)	17.11	0.89	0.3053	1.04 [0.57-1.90]
	dcSSc without PAH (n=164)	13.41	0.13	0.1633	0.78 [0.57-1.08]
	lcSSc without PAH (n=438)	15.41	0.38	0.09571	0.92 [0.76-1.11]
Norway	Controls (n=274)	15.88			
	dcSSc with PAH (n=0)	NA	NA	NA	NA
	lcSSc with PAH (n=9)	22.22	0.47	0.5789	1.51 [0.49-4.71]
	dcSSc without PAH (n=30)	16.67	0.87	0.3656	1.06 [0.52-2.17]
	lcSSc without PAH (n=57)	24.56	2.60E-2	0.247	1.73 [1.06-2.8]

*Unaffected controls are used as reference for each phenotype comparison. **Odds ratio (OR) for the minor allele. MAF, minor allele frequency; CI, confidence interval; SSc, systemic sclerosis; lcSSc, limited cutaneous systemic sclerosis; dcSSc, diffuse cutaneous systemic sclerosis; ACA+, patients with anti-centromere antibodies; ATA+, patients with anti-topoisomerase antibodies; PF+, patients affected by pulmonary fibrosis; PAH+, patients affected by pulmonary arterial hypertension.