

Supplementary table 1. Prevalence of clinical manifestations in the replication cohort (n=836)

Clinical Variable	n (%)
Male sex	44 (12)
ACR 1982 classification criteria[1]	
1 Malar rash	216 (59)
2 Discoid rash	40 (11)
3 Photosensitivity	265 (72)
4 Oral ulcer	109 (30)
5 Arthritis	301 (82)
6 Serositis	151 (41)
7 Renal disorder	144 (39)
8 Neurological disorder	40 (11)
9 Hematologic disorder	245 (68)
10 Immunologic disorder	305 (83)
Anti-dsDNA	175 (76)
11 ANA	371 (100)
Cardiovascular events	
MI	21 (6)
ICVD	33 (9)
VTE	61 (16)
Antiphospholipid antibodies	
Clinical APS	32 (14)
Anti-β2GP-I IgG	35 (18)
Anti-β2GP-I IgM	25 (13)
LA	86 (39)
aCL-IgG	65 (29)
aCL-IgM	55 (24)

OR: odds ratio. CI: Confidence interval. ACR: American College of Rheumatology[1]. dsDNA: double-stranded DNA. ANA: Antinuclear antibodies. MI: Myocardial infarction. ICVD: Ischemic cerebrovascular disease. VTE: venous thromboembolism. APS: antiphospholipid syndrome. LA: Lupus anticoagulant. Anti-β2GP-I: anti-β₂ Glycoprotein-I.

Supplementary table 2. The 60 SLE susceptibility SNPs investigated for associations with myocardial infarction in the discovery cohort.

Location	Lead SNP in publication[2]	Gene	Discovery cohort		Location	Lead SNP in publication[2]	Gene	Discovery cohort	
			OR	P				OR	p
1p13.2	rs2476601	<i>PTPN22</i>	1.53 (0.93-2.51)	0.097	6q23	rs6932056	<i>TNFAIP3</i>	0.73 (0.28-1.90)	0.52
1q23.3	rs1801274	<i>FCGR2A</i>	1.18 (0.80-1.74)	0.40	6q23	rs2327832	<i>OLIG3-LOC100130476</i>	1.15 (0.75-1.77)	0.52
1q25.1	rs2205960	<i>TNFSF4</i>	1.36 (0.89-2.09)	0.16	7p15.1	rs849142	<i>JAZF1</i>	1.10 (0.75-1.62)	0.61
1q25.3	rs17849502	<i>NCF2</i>	1.92 (1.05-3.53)	0.035	7p12.2	rs4917014	<i>IKZF1</i>	0.76 (0.49-1.18)	0.23
1q25.3	rs10911363	<i>NCF2</i>	0.88 (0.56-1.40)	0.59	7q11.23	rs73366469	<i>GTF2IRD1-GTF2I</i>	1.05 (0.62-1.79)	0.85
1q31.3	rs34889541 ^a	<i>CD45</i>	1.01 (0.40-2.54)	0.99	7q32.1	rs4728142	<i>TNPO3-IRF5</i>	1.00 (0.67-1.51)	0.99
1q32.1	rs3024505	<i>IL10</i>	0.92 (0.56-1.53)	0.76	7q32.1	rs2070197	<i>TNPO3-IRF5</i>	0.63 (0.37-1.04)	0.073

2p23.1	rs7579944	LBH	0.96 (0.62-1.47)	0.85	8p23.1	rs2980512 ^a	FAM86B3P	0.81 (0.54-1.22)	0.32
2p14	rs6740462	SPRED2	0.82 (0.51-1.31)	0.40	8p23.1	rs2736340	BLK	0.80 (0.52-1.24)	0.32
2q24.2	rs2111485	IFIH1	0.76 (0.49-1.17)	0.21	8q12	rs7829816	LYN	0.54 (0.34-0.85)	0.0087
2q24.2	rs10930046	IFIH1	1.44 (0.40-5.14)	0.58	8q21	rs1966115	PKIA-ZC2HC1A	1.09 (0.72-1.65)	0.69
2q32.3	rs11889341	STAT4	1.71 (1.15-2.55)	0.0084	10q11.23	rs877819	WDFY4	1.12 (0.74-1.71)	0.58
3p14.3	rs6445972	ABHD6-PXK	1.20 (0.74-1.95)	0.46	11p15.5	rs4963128	IRF7-PHRF1	1.06 (0.68-1.66)	0.78
3q13.33	rs1132200	TMEM39A	1.57 (0.80-3.06)	0.19	11p13	rs2732552	CD44	1.07 (0.72-1.57)	0.75
3q25.33	rs564799	IL12A	1.43 (0.95-2.15)	0.085	11q13.1	rs1308020 ^a	RNASEH2C	1.29 (0.83-1.99)	0.26
3q26.2	rs10936599	MYNN	0.59 (0.39-0.91)	0.016	11q13.4	rs3794060 ^a	DHCR7-NADSYN1	0.87 (0.57-1.32)	0.52
4q24	rs10028805	BANK1	1.05 (0.70-1.57)	0.83	11q24.3	rs7941765 ^a	ETS1-FLI1	1.03 (0.69-1.52)	0.90
4q27	rs907715	IL21	0.80 (0.52-1.24)	0.32	12q24.12	rs10774625	SH2B3-ATXN2	0.87 (0.58-1.30)	0.49
5q31.1	rs7726414	TCF7-SKP1	1.12 (0.38-3.32)	0.84	12q24.32	rs1059312	SLC15A4	0.86 (0.58-1.29)	0.47
5q33.1	rs7708392 ^a	TNIP1	1.31 (0.87-1.98)	0.19	16p13	rs9652601	CLEC16A-CIITA-SOCS1	1.33 (0.84-2.09)	0.23
5q33.3	rs2431697	PTTG1-MIR146A	0.85 (0.57-1.28)	0.44	16p11.2	rs34572943	ITGAM-ITGAX	0.77 (0.42-1.39)	0.38
6p23	rs17603856	ATXN1	1.20 (0.79-1.81)	0.39	16q13	rs223881	CCL22	1.00 (0.65-1.56)	0.99
6p21.31	rs11755393	UHRF1BP1	0.90 (0.61-1.32)	0.59	16q22.1	rs1170426 ^a	ZPF90	0.89 (0.55-1.45)	0.65
6p21.31	rs2762340	ANKS1A	1.10 (0.74-1.64)	0.65	16q24.1	rs2280381	IRF8	1.11 (0.72-1.70)	0.64
6p21.32-33	rs3906272 ^a	HLA-C-HLA-B	0.85 (0.49-1.48)	0.57	17q12	rs2941509	IKZF3	1.49 (0.68-3.24)	0.31
6p21.32-33	rs1269852	MSH5-ATF6B	0.59 (0.35-1.02)	0.058	17q25	rs930297	GRB2	0.55 (0.25-1.22)	0.14
6p21.32-33	rs9270984 ^a	HLA-DRB1	1.73 (0.99-3.03)	0.053	19p13	rs3093030	ICAM1-ICAM4-ICAM5	1.34 (0.91-1.99)	0.14
6p21.32-33	rs2051549 ^a	HLA-DQA2	0.76 (0.51-1.14)	0.18	19p13	rs2304256	TYK2	0.85 (0.55-1.32)	0.46
6q15	rs597325	BACH2	0.86 (0.57-1.29)	0.46	20q13.13	rs11697848	RNF114	0.83 (0.28-2.45)	0.74
6q21	rs6568431	PRDM1-ATG5	0.83 (0.54-1.27)	0.38	22q11.21	rs7444	UBE2L3-YDJC-HIC2	0.75 (0.46-1.22)	0.25

SNP: single nucleotide polymorphism. We selected SNPs with a $p < 5.0 \times 10^{-8}$ from Chen *et al.* [2]. All SNPs have previously reported genome-wide levels of significance for SLE ($p < 5 \times 10^{-8}$). ORs for MI are based on comparisons between the 61 patients with MI and 713 patients without MI in the discovery cohort. ^aFor SNPs not occurring on the ImmunoChip, the proxy SNP with the highest linkage disequilibrium[3] was used; for rs34889541, rs16843520 was used ($r^2=1.00$); for rs7708392, rs6889239 was used ($r^2=0.99$); for rs3906272, rs28732109 was used ($r^2=1.00$); for rs9270984, rs9270986 was used ($r^2=1.00$); for rs2051549, rs7453920 was used ($r^2=1.00$); for rs2980512, rs2948286 was used ($r^2=0.96$); for rs1308020, rs489574 was used ($r^2=1.00$); for rs3794060, rs4944062 was used ($r^2=1.00$); for rs7941765, rs6590343 was used ($r^2=0.99$); for rs1170426, rs1170427 was used ($r^2=1.00$).

Supplementary table 3 Interaction models including all patients (n=1277)

	Myocardial infarction		Nephritis ¹	
	OR (95% CI)	p	OR (95% CI)	P
Age at follow-up	1.07 (1.05-1.09)	2.5x10⁻¹³	0.97 (0.96-0.98)	1.0x10⁻¹²
Disease duration	1.03 (1.01-1.05)	0.0038	1.02 (1.01-1.04)	5.4x10⁻⁵
rs11889341 (STAT4)	1.22 (0.58-2.69)	0.61	0.80 (0.57-1.13)	0.20

Smoking²	1.07 (0.55-2.00)	0.84	1.00 (0.77-1.30)	0.99
rs11889341*smoking	2.14 (1.01-4.62)	0.049	1.53 (1.07-2.17)	0.020

OR: Odds ratio. STAT4: signal transducer and activator of transcription 4. Two separate logistic regression models, including a rs11889341*smoking interaction term, were performed for MI and nephritis. ¹Defined according to the 1982 ACR criteria[1]. ²Defined as ever-smoking, including both current and past smoking. p<0.05 (unadjusted) in bold

Supplementary table 4. Multiple regression model for myocardial infarction

	Smokers ¹		Non-smokers ¹	
	OR	p	OR	p
rs11889341 (STAT4) ²	3.26 (1.15-9.20)	0.026	0.58 (0.09-3.54)	0.55
Nephritis ³	0.89 (0.23-3.49)	0.87	5.54 (0.56-54.55)	0.14
Any aPL ⁴	0.68 (0.21-2.13)	0.50	2.04 (0.18-23.50)	0.60
Age at follow-up	1.09 (1.03-1.15)	0.0031	1.10 (1.02-1.20)	0.021
Disease duration	1.03 (0.97-1.09)	0.38	1.02 (0.95-1.09)	0.64

OR: Odds ratio. STAT4: Signal transducer and activator of transcription 4. aPL: anti-phospholipid antibodies. To test whether the association between STAT4 and MI in smokers remained significant after adjusting for aPL and nephritis, a multiple regression model was performed including all patients with available data for all included variables (n=152). A separate model was performed for the non-smokers (n=170). ¹Defined as ever-smoker, including current and past smokers, or never-smokers. ²OR per additional risk allele. ³Defined according to the 1982 ACR criterion (ref). ⁴Defined as having at least one positive aPL out of aCL (IgG or IgM), aβ₂GPI (IgG or IgM) or LA. p<0.05 (unadjusted) in bold

1. Tan EM, Cohen AS, Fries JF, et al. The 1982 revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1982;25:1271-7