A candidate gene study of the type I interferon pathway implicates *IKBKE* and *IL8* as risk loci for SLE

Johanna K. Sandling, Sophie Garnier, Snaevar Sigurdsson, Chuan Wang, Gunnel Nordmark, Iva Gunnarsson, Elisabet Svenungsson, Leonid Padyukov, Gunnar Sturfelt, Andreas Jönsen, Anders A. Bengtsson, Lennart Truedsson, Catharina Eriksson, Solbritt Rantapää-Dahlqvist, Anders Mälarstig, Rona J. Strawbridge, Anders Hamsten, Lindsey A. Criswell, Robert R. Graham, Timothy W. Behrens, Maija-Leena Eloranta, Gunnar Alm, Lars Rönnblom and Ann-Christine Syvänen

Supplementary information

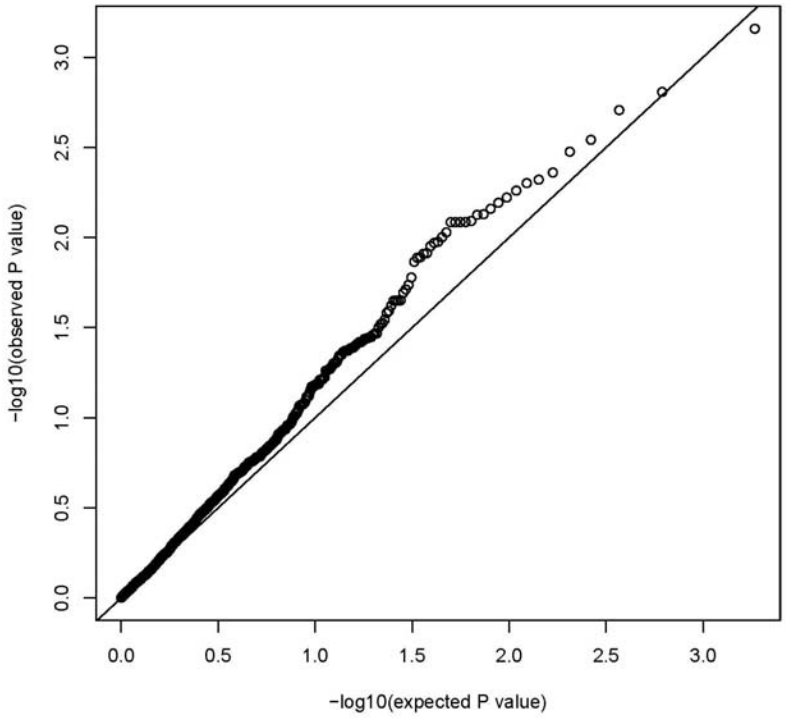

Figure S1 Q-Q plot of association results in the discovery phase. The observed P-values are plotted against the theoretical distribution, the deviation from the null distribution suggests the presence of multiple weak associations in the data. Only nine associated SNPs would be expected by chance with P values < 0.01, and after removal of the SNPs in the 14 genes included based on prior evidence for association to SLE, we observed 20 (P = 0.030, Fisher's exact test), which indicates the presence of true associations in our data.

Table S1 Number of SLE patients and controls analysed

	Discovery		*Confirmation*		*Replication*		*Total*	
	SLE	Ctrl	SLE	Ctrl	SLE	Ctrl	SLE	Ctrl
Sweden								
Uppsala	131	161	19	291	-	-	150	452
Stockholm	203	187	114	161	-	-	317	348
Lund	156	195	-	-	-	-	156	195
Umeå	-	-	260	520	-	-	260	520
(Broadbent *et al.* 2008)	-	-	-	673	-	-	0	673
US								
(Hom *et al.* 2008)	-	-	-	-	1 435	3 583	1 435	3 583
(Gateva *et al.* 2009)	-	-	-	-	-	4 564	0	4 564
Sum								
Pre-QC							2 318	10 335
Post-QC							2 136	9 694

Table S2 Sequences of primers used in the confirmatory phase. Sequences are given in the 5' to 3' direction. SNPs were genotyped in either 12 or 48-plex assays using the SNPstream system.

A PCR primers

SNP	*PCR forward primer*	*PCR reverse primer*
rs1539243	ARGTGAGGGAGTTTGAGGTC	CAAGCACCGGACCTACCG
rs17433930	TTACTGGCATCCTCAGAGCT	TTCTTTCCAGGAGCTCAGACT
rs3754974	TAGTTCCCTCCTTATCTTAGTCTAATAGC	GAAAATTATTTACCAGAAGCAGAAGT
rs13397244	GAAGTCAACCAGATTCCATTAATAGT	ATTTATTGAGACTTCTGAATATAAACCTAAG
rs12476789	ATGTCTTTGAGATCTATCTTGTCTCTC	CATCTCCCACTAAGTAGCAATGA
rs7600342	TTTCAATCCTTCAGGTAAGTATAAT	AATCCTGTGTTTCGGTCCT
rs3754972	AATAAACCAAGTTCTACTGGTTATTTC	AAAAAAGTACAAAGATTTTGACCAC
rs1267075	AATCCTTGACTGAAATGTCTTTAAATA	GGCTCCAGGAATGTACTTGTAA
rs3769972	ATAATTTCTAGACAAGAGCCAGAATTAT	TAAATGAAATGGCTCATTCAAA
rs10178063	TCCAATCTCCATTCAATCCTT	AGAGAGTGAAGGAAAGGAGCC
rs16833155	TGAAGGGCTTTAGGGTTGTAT	ATATTCAGCCATTTATTTTTGTTCTG
rs2030171	AGCAAAGAAAAGTCTTCTGCTC	TTTTCTAATCTGTGGGATGGG
rs10199181	ATTTAACCCTAAAAATTCCTTCTGT	TTATTGGTATTTAGAGAAGTAATAGAGACTAACT
rs16833172	TTTTTCAGTTCAGTTTTATTTTACCTG	TGGGTTCGCTTGGCTAAT
rs17817900	ATCCTCAAATCTTAATTGATTCTTCC	AATGGATTAAAAGGTAGATAAGGGC
rs4694178	AATTTAGTTTAGTGATGGTCTGGTG	ATATGCCAGCAAAAATACCTCTC
rs734187	AATATTCTGGGCATTGACTTAGC	TTTTCAAATTGACTTGCTTTCC
rs2269103	TAAATTCACTATCGGGGTTCTG	TTGCATATGTAGTAATGGTATTTTCATT
rs1331314	ACACACTACATTCTGATAACAAAGA	ATAAGAGTTTCAAATTGCATTAGATGT
rs2073320	GTGAAATAGAACATTTATAAAGGCG	AATTACCTTTCACATTTCGTTTGT
rs5030482	AAATTAAGGCTGATCTAYAACGCT	GAGACCCGCAACTAGTATAAGCT
rs5030472	TCCACCTCAAATCATCTACATTG	TGAAATAGTTTTCCAAGAAGACAAA
rs2303439	TTTAAACTGTATTGTCAATGGCTG	TTTCCTTTCTCTATAACTTTTGAAAGTAG
rs6503691	AAAGAAGCAAACAAGGAAAAATG	TGTTCTTCCTATTGTAATATGCAGTG
rs2289863	TACTACCCCTCCAATAAGCCC	TGACAGTGATGCGGTTGG

B Minisequencing primers

SNP	*Extension primer containing tag-sequence*	*Strand*	*Alleles*	*Assay*
rs1539243	CGCAGAAGCAACTCACTTCTTGCGGAAGCTGAACCACCAGAACAT	Forward	C/T	48-plex
rs17433930	AACATCCACGCAACTCATACAGTGGAAACAGGGAGATCTGGATTT	Forward	C/T	48-plex
rs3754974	CAGAACATCCTCAGAAGCAATCATGTATTTCATCTCTTTTTGCAT	Forward	C/T	48-plex
rs13397244	AGCAAGACCACCTAGACCAGGCACATCAAAGATTTGACTGAGAAC	Forward	C/T	12-plex
rs12476789	CGACTGTAGGTGCGTAACTCTTAAGATGATTAGAGTATTGATAGG	Forward	A/G	12-plex
rs7600342	AGCGATCTGCGAGACCGTATTTCATTTACAGAGGAAGAAACCAAA	Forward	A/G	12-plex
rs3754972	AGCGATCTGCGAGACCGTATAGTTTGATGTAATATTTCCTTTTGG	Forward	A/T	12-plex
rs1267075	CAGCCATCCATTCACTATCTACTTCTGCGGTGCTTTAAGTGTCTT	Forward	C/T	48-plex
rs3769972	ATCTAACGCACCTACGACCTGGTCACTTGGGAGAGAATATTATGT	Forward	C/T	48-plex
rs10178063	GCAAGCCATCAGCTAATACAGACTTGGGCTGAATTTAAACTC	Forward	C/T	48-plex
rs16833155	GGCTATGATTCGCAATGCTTCTGTAGGTACCCCAGATTTCTTGTG	Reverse	A/G	12-plex
rs2030171	GATCCATCAACAGACATCACCCCTTACTTGGACAACTGCTCACTC	Reverse	C/T	48-plex
rs10199181	GGCTATGATTCGCAATGCTTATGCTATATTTACTGATGCTGTAGA	Forward	A/T	12-plex
rs16833172	AGTAGCCTAACAGCACTCGAAGGCGTTGCAGCTCCCATTGCCTGA	Reverse	C/T	48-plex
rs17817900	AATAAGCTCACCACCGTCAAGCAGAAGGAGGCAGCAGAAGAGATG	Reverse	C/T	48-plex
rs4694178	ACGCACGTCCACGGTGATTTTTTCTCATTGGTTGTCCAAAGGAAG	Forward	A/C	12-plex
rs734187	AGACCGACAAGCAATCTACAGAGTCATGAATCTGGACTCCAAGTG	Reverse	C/T	48-plex
rs2269103	CAGCACTATTACCATCACGTTACTGACAATAACTTAATTGGGCCT	Reverse	C/T	48-plex
rs1331314	GCGGTAGGTTCCCGACATATAATGGTGCTGGGGTTTCTATACACT	Forward	CG	12-plex
rs2073320	CCACTCAACTCCACGAATACACATCTGGCAGAGTTACTGAGTCAC	Reverse	C/T	48-plex
rs5030482	CCATAACAACTTACCAGCCAAAGTTGTCTGGTAATGAGAGATGAC	Reverse	C/T	48-plex
rs5030472	CACTAGTCATAACGCAGCCTGATTTGAGGAACTACAAGTAGTTTGT	Reverse	C/T	48-plex
rs2303439	ACAACTCACGCAAGTACCATTGATGGTTTATGCTGCACCTATTCA	Reverse	C/T	48-plex
rs6503691	CAGAATAGCCACGCCTAGATTTTGGCTGTGACATAAAGATTAATG	Reverse	C/T	48-plex
rs2289863	CACCGCTATCAACAGACTTGGGCCGTGCCGCCCCATCAACCTCAC	Forward	C/T	48-plex

Table S3 List of IFN related genes included in the discovery phase[1]

A TLRs and intracellular sensors and their signaling pathways and transcription factors, with a focus on PDC and regulation of IFN-genes

Gene	*Location*	*SNP with lowest P*	P_{Chi2}	*Comment*
AZI2	chr3:p24.1	rs12054402	0.20	
DDX58/RIG-I	chr9:p21.1	rs4013911	0.026	
DHX58/LGP2	chr17:q21.2	rs2074159	0.11	
FADD	chr11:q13.3	rs10898853	0.17	
IKBKe	chr1:q32.1	rs1539243	0.0033	
IRAK4	chr12:q12	rs4251520	0.44	
IRF1	chr5:q23.3	rs12657912	0.29	
IRF2	chr4:q35.1	rs17075769	0.011	
IRF3	chr19:q13.33	rs2304207	0.29	
IRF4	chr6:p25.3	rs6899334	0.022	
MyD88	chr3:p22.3	rs4988457	0.33	
RIPK2	chr8:q21.3	rs390993	0.23	
SPP1	chr4:q22.1	rs1126616	0.29	
TANK	chr2:q24.2	rs3754974	0.0055	
TBK1	chr12:q14.2	rs7298692	0.45	
TIRAP	chr11:q24.2	rs1786704	0.183	
TLR3	chr4:q35.1	rs7657186	0.33	
TLR4	chr9:q33.1	rs5030717	0.19	
TLR5	chr1:q41	NA	NA	Failed assay design
TLR7	chrX:p22.2	rs1638596	0.067	
TLR8	chrX:p22.2	rs2109134	0.43	
TLR9	chr3:p21.2	rs352140	0.64	
TRAF3	chr14q:32.32	rs10137035	0.02	
TRAF6	chr11:p12	rs5030482	0.0029	
TRAM1	chr8:q13.3	rs28491596	0.12	
TRIF/TICAM1	chr19:p13.3	rs7255265	0.18	
VISA	chr20:p13	rs7262903	0.11	

B Functionally important membrane molecules on PDC

Gene	*Location*	*SNP with lowest P*	P_{Chi2}	*Comment*
CLEC4C/CLECSF7	chr12:p13.31	rs6488610	0.018	
CXCR3	chrX:q13.1	rs2280964	0.41	
CXCR4	chr2:q21.3	rs2228014	0.077	
FCGR2A	chr1:q23.3	rs1801274	0.18	
FCGR2B	chr1:q23.3	rs2333845	0.11	
NRP1	chr10:p11.22	rs1331314	0.0020	

C Type I IFN and other cytokine genes regulated via TLR and RLR pathways

Gene	*Location*	*SNP with lowest P*	P_{Chi2}	*Comment*
CXCL11	chr4:q21.1	rs7436646	0.36	
CXCL12	chr10:q11.21	rs2839695	0.080	
CXCL9	chr4:q21.1	rs3733236	0.060	
IFNA1	chr9:p21.3	rs1332190	0.67	
IFNA2	chr9:p21.3	rs615544	0.18	
IFNA4	chr9:p21.3	rs2383183	0.025	
IFNA5	chr9:p21.3	rs7021906	0.14	
IFNA6	chr9:p21.3	rs614541	0.23	
IFNA7	chr9:p21.3	rs28368137	0.34	
IFNA8	chr9:p21.3	rs1330322	0.067	
IFNA10	chr9:p21.3	rs12555631	0.32	
IFNA13	chr9:p21.3	rs643070	0.045	
IFNA14	chr9:p21.3	rs28368137	0.34	
IFNA16	chr9:p21.3	rs10964912	0.97	
IFNA17	chr9:p21.3	rs10964920	0.14	
IFNA21	chr9:p21.3	rs7047299	0.042	
IFNB1	chr9:p21.3	rs1051922	0.29	
IFNE1	chr9:p21.3	rs1556461	0.083	
IFNK	chr9:p21.2	rs4879540	0.26	
IFNW1	chr9:p21.3	rs10757189	0.036	
IL28A	chr19:q13.2	NA	NA	Failed genotyping QC
IL28B	chr19:q13.2	NA	NA	Failed genotyping QC
IL29	chr19:q13.2	rs7247086	0.12	

D Genes involved in response to type I and III IFN (mediation and regulation)

Gene	*Location*	*SNP with lowest P*	P_{Chi2}	*Comment*
IFNAR1	chr21:q22.11	rs17875880	0.18	
IFNAR2	chr21:q22.11	rs16990416	0.12	
IL10RB	chr21:q22.11	NA	NA	Failed assay design
IL28RA	chr1:p36.11	rs3932667	0.46	
IRF9/ISGF3G	chr14:q11.2	rs2236350	0.16	
JAK1	chr1:p31.3	rs4916004	0.039	
PIAS1	chr15:q23	rs8025474	0.042	
PIAS2	chr18:q21.1	rs3786258	0.38	
PIAS3	chr1:q21.1	rs17352344	0.22	
PIAS4	chr19:p13.3	rs2289863	0.00069	
SOCS1	chr16:p13.13	rs193779	0.24	
SOCS3	chr17:q25.3	rs8064821	0.88	
STAT1	chr2:q32.2	rs10199181	0.0016	
STAT2	chr12:q13.3	rs2066807	0.75	
STAT3	chr17:q21.2	rs17880368	0.019	
STAT5A	chr17:q21.2	rs8068688	0.74	
STAT5B	chr17:q21.2	rs6503691	0.013	

E Genes regulated by type I IFN

Gene	*Location*	*SNP with lowest P*	P_{Chi2}	*Comment*
CXCL10	chr4:q21.1	rs3921	0.35	
TNFSF11	chr13:q14	rs9594782	0.076	
TNFSF13B	chr13:q32-q34	rs9520835	0.032	
TNFSF13	chr17:p13.1	rs12942687	0.52	
TNFRSF13B	chr17:p11.2	rs4985700	0.094	
TNFRSF17	chr16:p13.1	rs11570158	0.27	
TNFRSF13C	chr22:q13.1-q13.31	rs7290134	0.43	

F Other genes

Gene	*Location*	*SNP with lowest P*	P_{Chi2}	*Comment*
DQX1	chr2:p13.1	rs6709863	0.035	
RALBP1	chr18:p11.22	rs17508182	0.076	

G Genes that had published association to SLE

Gene	*Location*	*SNP with lowest P*	P_{Chi2}	*Comment*
ACE	chr17:q23.3	rs4267385	0.15	
C6orf125	chr6:p21.31	rs594223	0.050	
CCL2	chr17:q12	rs3760396	0.33	
CRP	chr1:q23.2	rs1800947	0.33	
CTLA4	chr2:q33.2	rs231779	0.21	
DNASE1	chr16:p13.3	rs1053874	0.90	
FCRL3	chr1:q23.1	rs7528684	0.19	
IL1A	chr2:q13	rs1800587	0.89	
IL1RN	chr2:q13	rs380092	0.18	
IL6	chr7:p15.3	rs1474348	0.036	
IL8	chr4:q13.3	rs4694178	0.0048	
ITPR3	chr6:p21.31	rs2296329	0.039	
MBL2	chr10:q21.1	rs10824793	0.26	
PADI4	chr1:p36.13	rs2240340	0.96	

[1] 482 Swedish SLE cases and 536 controls.

Table S4 The most promising SNPs in the eight genes identified in the discovery phase[1] (SNPs with P<0.05). The rs-number of the SNP with the lowest p-value in each gene is indicated in bold. Independence of association signals within the same gene was investigated with a conditional analysis accounting for the most strongly associated SNP in each gene.

Gene	*Chr*	*SNP*	*Position*	$P_{logistic}$	$P_{conditional}$	r^2	*Confirmatory phase*
IKBKE	1	**rs1539243**	203036182	0.0036	NA	1	Genotyped
IKBKE	1	rs17433930	203041134	0.011	0.28	0.33	Genotyped
TANK	2	rs3820998	161820633	0.0089	NA	0.99	
TANK	2	**rs3754974**	161838462	0.0062	NA	1	Genotyped
TANK	2	rs13397244	161839598	0.0067	NA	0.99	Genotyped
TANK	2	rs1267076	161848164	0.028	0.056	0.01	
TANK	2	rs12476789	161852196	0.0089	NA	0.99	Genotyped
TANK	2	rs1267078	161857178	0.036	0.063	0.01	
TANK	2	rs1267080	161864079	0.039	0.069	0.01	
TANK	2	rs16845704	161875201	0.038	1.00	0.94	
TANK	2	rs7600342	161880718	0.015	NA	0.99	Genotyped
TANK	2	rs3754972	161882525	0.0089	NA	0.99	Genotyped
TANK	2	rs3769975	161883914	0.024	0.81	0.87	
TANK	2	rs1267075	161885324	0.029	0.052	0.01	Genotyped
TANK	2	rs3769973	161889981	0.0081	NA	0.99	
TANK	2	rs3769972	161893004	0.011	NA	1	Genotyped
TANK	2	rs10178063	161899325	0.0089	NA	0.99	Genotyped
TANK	2	rs12471074	161914481	0.024	0.64	0.86	
TANK	2	rs3754971	161917272	0.024	0.81	0.87	
STAT1	2	rs1547550	191671231	0.015	0.41	0.29	
STAT1	2	rs2280232	191676272	0.044	0.029	0.01	
STAT1	2	rs7562024	191681027	0.048	0.97	0.37	
STAT1	2	rs16833155	191686883	0.0097	0.049	0.05	Failed genotyping
STAT1	2	rs10173099	191692838	0.0071	0.90	0.71	
STAT1	2	rs2030171	191694669	0.0036	0.51	0.71	Genotyped
STAT1	2	**rs10199181**	191699059	0.0013	NA	1	Failed genotyping
STAT1	2	rs16833172	191701575	0.0067	0.022	0.02	Genotyped
STAT1	2	rs17817900	191705373	0.011	0.037	0.02	Failed genotyping
STAT1	2	rs1467199	191706008	0.028	0.87	0.43	
IL8	4	**rs4694178**	74977723		NA	1	Genotyped
NRP1	10	rs2474726	33523567	0.039	0.44	0.20	
NRP1	10	rs734187	33524702	0.046	0.47	0.20	Genotyped
NRP1	10	rs2269103	33539226	0.012	0.31	0.90	Genotyped
NRP1	10	rs3904032	33560274	0.015	0.36	0.91	
NRP1	10	**rs1331314**	33564687	0.0023	NA	1	Genotyped
NRP1	10	rs11009314	33570967	0.0074	0.52	0.95	
NRP1	10	rs2073320	33593263	0.037	0.020	0.00	Genotyped
TRAF6	11	**rs5030482**	36466602	0.0028	NA	1	Genotyped
TRAF6	11	rs5030472	36470362	0.036	0.67	0.61	Genotyped
TRAF6	11	rs2303439	36470866	0.018	0.42	0.82	Failed genotyping
STAT5B	17	**rs6503691**	37647616	0.0100	NA	1	Genotyped
PIAS4	19	**rs2289863**	3979783	0.00099	NA	1	Genotyped

$P_{logistic}$ is the p-value for a logistic regression analysis under an additive model.

$P_{conditional}$ is the p-value in a additive logistic regression analysis conditioning on the best SNP in the gene.

r^2 is the pair-wise LD with the SNP with the lowest p-value in the gene.

[1] 482 Swedish SLE cases and 536 controls.

Table S5 Results of the combined analysis for the Swedish discovery and confirmation SLE cohorts[1]

Gene	*CHR*	*SNP*	*bp*	*Minor/major alleles*	*MAF cases*	*MAF controls*	$P_{SNPtest}$	*Risk allele*	*OR (95% CI)*	$P_{logistic}$	$P_{conditional}$
IKBKE	1	rs1539243	204714410	T/C	0.16	0.18	**0.031**	C	1.19 (1.02-1.39)	0.029	0.51
IKBKE	1	rs17433930	204719362	G/A	0.07	0.09	**0.013**	A	1.33 (1.06-1.67)	0.011	NA
TANK	2	rs3754974	161721201	G/A	0.05	0.04	**0.0087**	G	1.44 (1.09-1.89)	0.0080	NA
TANK	2	rs13397244	161722337	G/A	0.05	0.04	**0.010**	G	1.42 (1.08-1.86)	0.0092	NA
TANK	2	rs12476789	161734935	G/A	0.05	0.04	**0.019**	G	1.38 (1.05-1.81)	0.017	NA
TANK	2	rs7600342	161763457	G/A	0.05	0.04	**0.049**	G	1.39 (1.06-1.82)	0.016	NA
TANK	2	rs3754972	161765264	A/T	0.05	0.04	**0.010**	A	1.42 (1.08-1.86)	0.0094	NA
TANK	2	rs1267075	161768063	G/A	0.19	0.18	0.75	G	1.02 (0.88-1.19)	0.77	0.61
TANK	2	rs3769972	161775743	G/A	0.05	0.04	**0.018**	G	1.38 (1.05-1.81)	0.017	NA
TANK	2	rs10178063	161782064	G/A	0.05	0.04	**0.0078**	G	1.44 (1.10-1.89)	0.0072	NA
STAT1	2	rs2030171	191577408	A/G	0.35	0.29	**1.2E-05**	A	1.31 (1.16-1.49)	1.0E-05	NA
STAT1	2	rs16833172	191584314	A/G	0.04	0.03	**0.015**	A	1.51 (1.09-2.09)	0.012	0.16
IL8	4	rs4694178	74831552	C/A	0.52	0.46	**5.2E-05**	C	1.26 (1.12-1.42)	6.1E-05	-
NRP1	10	rs734187	33524702	A/G	0.24	0.24	0.67	A	1.03 (0.90-1.18)	0.65	-
NRP1	10	rs2269103	33539226	T/G	0.11	0.11	0.31	T	1.10 (0.92-1.33)	0.34	-
NRP1	10	rs1331314	33564687	G/C	0.11	0.10	0.32	G	1.11 (0.92-1.34)	0.30	-
NRP1	10	rs2073320	33593263	A/G	0.38	0.37	0.42	A	1.05 (0.93-1.18)	0.43	-
TRAF6	11	rs5030482	36466602	C/T	0.12	0.14	**0.0094**	T	1.25 (1.05-1.49)	0.012	NA
TRAF6	11	rs5030472	36470362	T/C	0.09	0.12	**0.013**	C	1.28 (1.05-1.55)	0.012	0.50
STAT5B	17	rs6503691	37647616	T/C	0.09	0.10	0.44	C	1.08 (0.88-1.32)	0.38	-
PIAS4	19	rs2289863	3979783	C/T	0.27	0.29	0.19	T	1.09 (0.96-1.25)	0.18	-

[1]826 Swedish cases and 1 835 controls genotyped in the discovery and replication phases including controls genotyped on the 1M chip

Genotypes for rs17433930, rs3754974, rs13397244, rs12476789, rs7600342, rs3754972, rs10178063, rs2030171, rs16833172, rs4694178, rs734187, rs1331314 and rs5030482 were imputed in the Swedish control genotyped on the 1M chip

MAF= Minor Allele Frequency, NA= Not Available, CI= Confidence Interval

$P_{conditional}$ on the SNP with lowest P-value in each gene: IKBKE-rs17433930, TANK-rs10178063, STAT1-rs2030171 and TRAF6-rs5030482.

Table S6 Complete results of the meta-analysis of the Swedish and US cohorts

			Combined Swedish dataset[1]					US dataset[2]					Meta-analysis[5]				
Gene	*SNP*	*Alleles*	*Risk allele*	*MAF cases*	*MAF controls*	*P*[3]	*OR (95% CI)*	*Risk allele*	*MAF cases*	*MAF controls*	*P*[3]	*OR (95% CI)*[4]	*Risk allele*	*P*	*Corrected P*[6]	*OR (95% CI)*[4]	*Hetero-geneity*[7]
IKBKE	rs1539243	T/C	C	0.16	0.18	**0.031**	1.19 (1.02-1.39)	C	0.14	0.17	**0.0028**	1.20 (1.07-1.35)	C	**2.6E-04**	**0.0054**	1.19 (1.09-1.31)	0.95
IKBKE	rs17433930	G/A	A	0.07	0.09	**0.013**	1.33 (1.06-1.67)	A	0.06	0.07	**0.0021**	1.33 (1.11-1.58)	A	**1.0E-04**	**0.0022**	1.33 (1.16-1.53)	0.99
TANK	rs3754974	G/A	G	0.05	0.04	**0.0087**	1.44 (1.09-1.89)	NA	0.04	0.04	0.98	0.99 (0.80-1.22)	NA	0.22	1.0	1.13 (0.96-1.34)	0.033
TANK	rs13397244	G/A	G	0.05	0.04	**0.010**	1.42 (1.08-1.86)	NA	0.04	0.04	0.98	0.99 (0.80-1.22)	NA	0.23	1.0	1.13 (0.96-1.33)	0.038
TANK	rs12476789	G/A	G	0.05	0.04	**0.019**	1.38 (1.05-1.81)	NA	0.04	0.04	0.96	0.99 (0.80-1.23)	NA	0.29	1.0	1.12 (0.95-1.32)	0.063
TANK	rs7600342	G/A	G	0.05	0.04	**0.049**	1.39 (1.06-1.82)	NA	0.04	0.04	0.87	0.95 (0.76-1.19)	NA	0.43	1.0	1.09 (0.92-1.29)	0.037
TANK	rs3754972	A/T	A	0.05	0.04	**0.010**	1.42 (1.08-1.86)	NA	0.04	0.04	0.95	0.96 (0.77-1.20)	NA	0.24	1.0	1.12 (0.94-1.32)	0.028
TANK	rs1267075	G/A	G	0.19	0.18	0.75	1.02 (0.88-1.19)	NA	0.17	0.17	0.87	0.99 (0.89-1.11)	NA	0.99	1.0	1.00 (0.92-1.10)	0.71
TANK	rs3769972	G/A	G	0.05	0.04	**0.018**	1.38 (1.05-1.81)	NA	0.04	0.04	0.95	0.96 (0.77-1.20)	NA	0.29	1.0	1.10 (0.93-1.30)	0.043
TANK	rs10178063	G/A	G	0.05	0.04	**0.0078**	1.44 (1.10-1.89)	NA	0.04	0.04	0.93	0.95 (0.77-1.19)	NA	0.23	1.0	1.11 (0.94-1.32)	0.019
STAT1	rs2030171	A/G	A	0.35	0.29	**1.2E-05**	1.31 (1.16-1.49)	A	0.37	0.34	**0.018**	1.11 (1.02-1.21)	A	**3.3E-05**	**6.9E-04**	1.17 (1.09-1.26)	0.029
STAT1	rs16833172	A/G	A	0.04	0.03	**0.015**	1.51 (1.09-2.09)	A	0.03	0.02	0.16	1.23 (0.95-1.59)	A	**0.016**	0.34	1.33 (1.09-1.63)	0.34
IL8	rs4694178	C/A	C	0.52	0.46	**5.2E-05**	1.26 (1.12-1.42)	C	0.43	0.41	0.064	1.13 (1.04-1.23)	C	**4.0E-04**	**0.0084**	1.17 (1.10-1.26)	0.12
NRP1	rs734187	A/G	A	0.24	0.24	0.67	1.03 (0.90-1.18)	NA	0.25	0.25	0.66	1.01 (0.92-1.12)	A	0.56	1.0	1.02 (0.94-1.10)	0.80
NRP1	rs2269103	T/G	T	0.11	0.11	0.31	1.10 (0.92-1.33)	T	0.11	0.10	0.065	1.11 (0.97-1.28)	T	**0.036**	0.75	1.11 (1.00-1.24)	0.96
NRP1	rs1331314	G/C	G	0.11	0.10	0.32	1.11 (0.92-1.34)	G	0.12	0.11	0.11	1.11 (0.97-1.26)	G	0.061	1.0	1.11 (1.00-1.23)	0.99
NRP1	rs2073320	A/G	A	0.38	0.37	0.42	1.05 (0.93-1.18)	NA	0.38	0.39	0.61	0.98 (0.90-1.06)	NA	0.94	1.0	1.00 (0.94-1.07)	0.35
TRAF6	rs5030482	C/T	T	0.12	0.14	**0.0094**	1.25 (1.05-1.49)	T	0.13	0.14	0.12	1.10 (0.97-1.24)	T	**0.0097**	0.20	1.14 (1.03-1.26)	0.22
TRAF6	rs5030472	T/C	C	0.09	0.12	**0.013**	1.28 (1.05-1.55)	C	0.11	0.11	0.19	1.09 (0.96-1.25)	C	**0.020**	0.42	1.15 (1.03-1.28)	0.20
STAT5B	rs6503691	T/C	C	0.09	0.10	0.44	1.08 (0.88-1.32)	NA	0.11	0.11	0.78	0.98 (0.86-1.12)	NA	0.91	1.0	1.01 (0.90-1.13)	0.44
PIAS4	rs2289863	C/T	T	0.27	0.29	0.19	1.09 (0.96-1.25)	NA	0.26	0.26	0.72	0.98 (0.89-1.08)	NA	0.76	1.0	1.02 (0.95-1.10)	0.19

[1]826 Swedish cases and 1 835 controls genotyped in the discovery and replication phases including controls genotyped on the 1M chip, P-values calculated using SNPtest

[2]1 310 US SLE cases and 7 859 controls genotyped in a GWAS. Genotypes for rs17433930, rs3754974, rs13397244, rs12476789, rs7600342, rs3754972, rs3769972, rs10178063, rs2030171, rs16833172, rs4694178, rs734187, rs2269103, rs1331314 and rs5030482 were imputed in this dataset as described in Gateva*et al* . P-values calculated using SNPtest

[3]P-value calculated using SNPtest

[4]Odds ratios are calculated relative to the risk allele defined in the analysis of the combined Swedish cohort

[5]Meta-analysis including 2 136 SLE cases and 9 694 controls

[6]P-value corrected for the 21 tested SNPs

[7]P-value test for heterogeneity of odds ratios

MAF= Minor Allele Frequency, NA= Not Available, CI= Confidence Interval