Figure S1. Examples of the DNA sequencing chromatograms for *PSMA6*: rs2277460 (A1: genotype CC; A2: genotype CA) and rs1048990 (B1: CC; B2: GG), *PSMC6*: rs2295826 (C1: AA; C2: GG) and rs2295827 (D1: CC; D2: TT) and *PSMA3* rs2348071 (E1: GG; E2: AA) described in the present study. On chromatograms, the sites of localization of the studied SNPs are marked in grey. Allelic variants in the sequence are in bold and underlined.
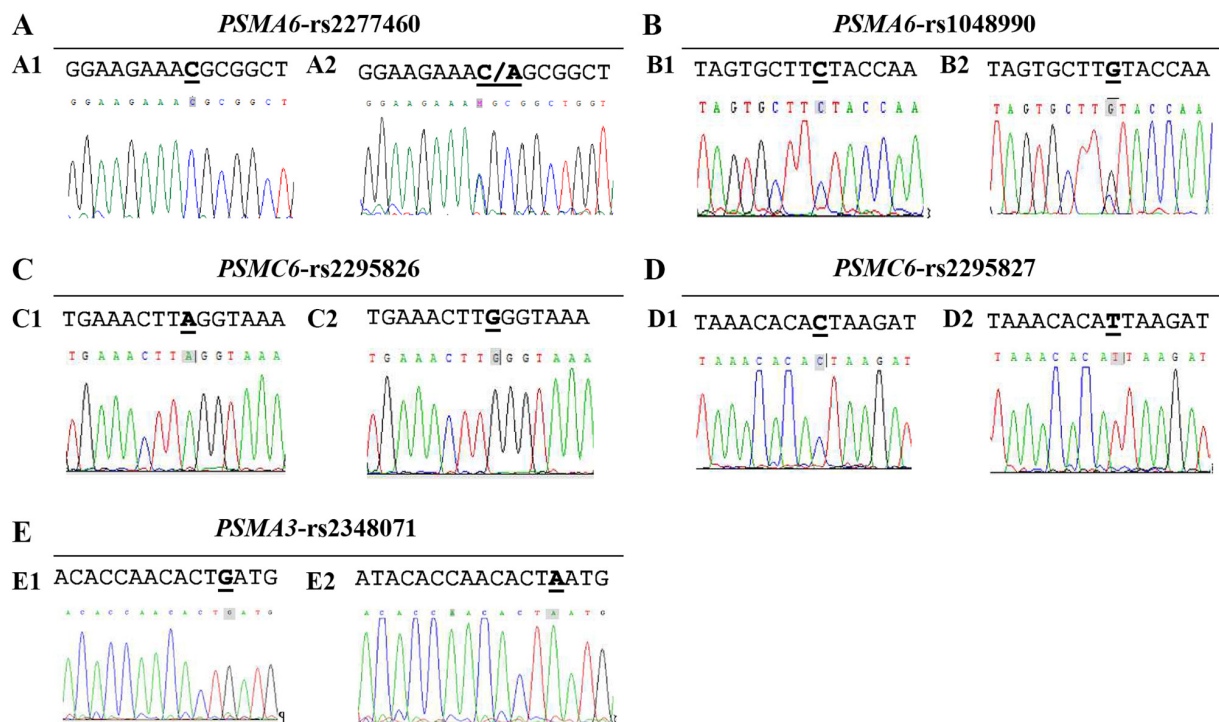
A   *PSMA6*-rs2277460

A1   GGAAGAAA**C**GCGGCT   A2   GGAAGAAA**C/A**GCGGCT

B   *PSMA6*-rs1048990

B1   TAGTGCTT**C**TACCAA   B2   TAGTGCTT**G**TACCAA

C   *PSMC6*-rs2295826

C1   TGAAACTT**A**GGTAAA   C2   TGAAACTT**G**GGTAAA

D   *PSMC6*-rs2295827

D1   TAAACACA**C**TAAGAT   D2   TAAACACA**T**TAAGAT

E   *PSMA3*-rs2348071

E1   ACACCAACACT**G**ATG   E2   ATACACCAACACT**A**ATG

Table SI. 14q SNP gentoype polymorphisms and correlation with gene expression level (profile) of related genes, including: (1) genes-candidates for MS and (2) IFN α/β signalling pathway genes, for HapMap unrelated subjects of CEU, YRI, HCB and JPT HapMap populations grouped in one HapMap unrelated subjects cohort.

A, rs1048990 (C/G) with MS susceptible genes; Genetic model, D; Genetic Factor, G

Genotype number (frequency)	Gene symbol	Chr. locus	Correlation between genotype and gene expression		
			Expression chip probe GI	Expression level (mean ± SD)	P-value
-	CD6	11q12.2	GI_5802993-S	-	n/s
CC 137 (0.65)	CD58	1p13.1	GI_4502676-S	11.82±0.24	0.0040[a]-
CG 58 (0.28)	-	-	-	11.92±0.23	-
GG 14 (0.07)	-	-	-	11.96±0.26	-
CC 137 (0.65)	HLA-A	6p22.1	GI_24797066-S	12.14±1.54	0.041[a]-
CG 58 (0.28)	-	-	-	11.65±1.75	-
GG 14 (0.07)	-	-	-	11.72±1.51	-
-	HLA-B	6p21.33	GI_21327676-S	-	n/s
-	HLA-DRB1	6p21.32	GI_4504410-S	-	n/s
-	IL2RA	10p15.1	GI_4557666-S	-	n/s
CC 137 (0.65)	IL7R	5p13.2	GI_28610150-S	6.29±0.21	0.042[a]-
CG 58 (0.28)	-	-	-	6.23±0.13	-
GG 14 (0.07)	-	-	-	6.22±0.17	-
-	IL12A	3q25.33	GI_24430218-S	-	n/s
-	IRF8 (ICSBP)	16q24.1	GI_4504566-S	-	n/s
CC 137 (0.65)	STAT3	17q21.2	GI_21618337-A	11.06±0.38	0.041[a]
CG 58 (0.28)	-	-	-	11.15±0.36	-
GG 14 (0.07)	-	-	-	11.28±0.56	-
-	TNFRSF1A	12p13.31	GI_23312372-S	-	-
CC 137 (0.65)	TNFRSF5 (CD40)	20q13.12	GI_23312370-A	9.91±0.35	0.0019[a]
CG 58 (0.28)	-	-	-	10.09±0.39	
GG 14 (0.07)	-	-	-	10.02±0.32	-

B, rs1048990 with IFN α/β signalling pathway genes; Genetic model, D; Genetic factor, G

Genotype number (frequency)	Gene symbol	Chr. locus	Correlation between genotype and gene expression		
			Expression chip probe GI	Expression level (mean ± SD)	P-value
	IFI6 (G1P3)	1p36.11	GI_13259551-A	-	n/s
CC 137 (0.65)	IFNA1 (IFN-α)	9p21.3	GI_13128949-S	5.88±0.09	0.0021[a]
CG 58 (0.28)	-	-	-	5.93±0.10	-
GG 14 (0.07)	-	-	-	5.90±0.08	-
-	IFNAR1	21q22.11	GI_10835182-S	-	n/s
-	IFNAR2	21q22.11	GI_19923128-S	-	n/s
-	IFNB1	9p21.3	GI_4504602-S	-	n/s
CC 137 (0.65)	IRF1	5q31.1	GI_4504720-S	10.67±0.32	0.035[a]
CG 58 (0.28)	-	-	-	10.78±0.34	-
GG 14 (0.07)	-	-	-	10.73±0.38	-
-	IRF2	4q35.1	GI_4755144-S	-	n/s
-	ISG15 (G1P2)	1p36.33	GI_4826773-S	-	n/s
-	ISG54 (IFIT2)	10q23.31	GI_34222091-S	-	n/s
-	ISGF3 (IRF9)	14q12	GI_25282406-S	-	n/s
-	JAK1	1p31.3	GI_4504802-S	-	n/s
-	PML (MYL)	15q24.1	GI_15451762-I	-	n/s
-	PML (MYL)	15q24.1	GI_15451776-A	-	n/s
-	PRMT1 (HRMT1L2)	19q13.33	GI_38195083-I	-	n/s
-	PRMT1 (HRMT1L2)	19q13.33	GI_38195086-A	n/s	
CC 137 (0.65)	PTP-1B (PTPN1)	20q13.13	GI_18104977-S	11.06±0.23	0.015[a]-
CG 58 (0.28)	-	-	-	11.12±0.25	-

Table SI. Continued.

B, rs1048990 with IFN α/β signalling pathway genes; Genetic model, D; Genetic factor, G

Genotype number (frequency)	Gene symbol	Chr. locus	Correlation between genotype and gene expression		
			Expression chip probe GI	Expression level (mean ± SD)	P-value
GG 14 (0.07)	-	-	-	11.22±0.26	-
-	*SHP-1 (PTPN6)*	12p13.31	GI_34328901-A	-	n/s
-	*SHP-1 (PTPN6)*	12p13.31	GI_34328901-I	-	n/s
-	*SHP-1 (PTPN6)*	12p13.31	GI_34328902-I	-	n/s
-	*SHP-2 (PTPN11)*	12q24.13	GI_33356176-S	-	n/s
-	SOCS1	16p13.13	GI_4507232-S	-	n/s
-	STAT1	2q32.2	GI_21536299-I	-	n/s
-	STAT1	2q32.2	GI_21536300-A	-	n/s
-	STAT1	2q32.2	GI_21536300-I	-	n/s
-	STAT2	12q13.3	GI_38202247-S	-	n/s
CC 137 (0.65)	TYK2	19p13.2	GI_34222294-S	9.84±0.25	0.001[a]
CG 58 (0.28)	-	-	-	9.76±0.27	-
GG 14 (0.07)	-	-	-	9.77±0.24	-
CC 137 (0.65)	USP18	22q11.21	GI_32313609-S	9.76±0.58	0.001[a]-
CG 58 (0.28)	-	-	-	10.08±0.55	-
GG 14 (0.07)	-	-	-	9.84±0.48	-

C, rs2295826 (A/G) with MS susceptible genes; Genetic Model, D; Genetic Factor, G

Genotype number (frequency)	Gene symbol	Chr. locus	Correlation between genotype and gene expression		
			Expression chip probe GI	Expression level (mean ± SD)	P-value
-	CD6	11q13	GI_5802993-S	-	n/s
-	*CD40 (TNFRSF5)*	20q13.12	GI_23312370-A	-	n/s
AA 152 (0.72)	CD58	1p13.1	GI_4502676-S	11.88±0.24	0.048[a]
AG 56 (0.27)	-	-	-	11.80±0.25	-
GG 2 (0.01)	-	-	-	11.96±0.38	-
-	HLA-A	6p22.1	GI_24797066-S	n/s	
AA 152 (0.72)	HLA-B	6p21.33	GI_21327676-S	14.31±0.27	0.004[a]-
AG 56 (0.27)	-	-	-	14.42±0.25	-
GG 2 (0.01)	-	-	-	14.65±0.56	-
-	HLA-DRB1	6p21.32	GI_4504410-S	-	n/s
-	IL2RA	10p15.1	GI_4557666-S	-	n/s
-	IL7R	5p13.2	GI_28610150-S	-	n/s
-	IL12A	3q25.33	GI_24430218-S	-	n/s
-	*IRF8 (ICSBP1)*	16q24.1	GI_4504566-S	-	n/s
AA 152 (0.72)	STAT3	17q21.2	GI_21618337-A	11.06±0.39	0.019[a]-
AG 56 (0.27)	-	-	-	11.18±0.37	-
GG 2 (0.01)	-	-	-	11.66±0.56	-
-	TNFRSF1A	12p13.31	GI_23312372-S	-	n/s

D, rs2295826 (A/G) with IFN α/β signaling pathway genes; Genetic Model, D; Genetic Factor, G

Genotype number (frequency)	Gene symbol	Chr. locus	Correlation between genotype and gene expression		
			Expression chip probe GI	Expression level (mean ± SD)	P-value
AA 152 (0.72)	*IFI6 (G1P3)*	1p36.11	GI_13259551-A	12.52±0.58	0.041[a]-
AG 56 (0.27)	-	-	-	12.67±0.46	-
GG 2 (0.01)	-	-	-	13.34±0.20	-

Table SI. Continued.

D, rs2295826 (A/G) with IFN α/β signaling pathway genes; Genetic Model, D; Genetic Factor, G

Genotype number (frequency)	Gene symbol	Chr. locus	Correlation between genotype and gene expression		
			Expression chip probe GI	Expression level (mean ± SD)	P-value
-	*IFNA1*	9p21.3	GI_13128949-S	-	-
-	*IFNAR1*	21q22.11	GI_10835182-S	-	-
-	*IFNAR2*	21q22.11	GI_19923128-S	-	-
-	*IFNB1*	9p21.3	GI_4504602-S	-	-
-	*IRF1*	5q31.1	GI_4504720-S	-	-
AA 152 (0.72)	*IRF2*	4q35.1	GI_4755144-S	7.66±0.36	0.026[a]-
AG 56 (0.27)	-	-	-	7.80±0.44	-
GG 2 (0.01)	-	-	-	7.81±0.56	-
-	*ISG15 (G1P2)*	1p36.33	GI_4826773-S	-	n/s
-	*ISG54 (IFIT2)*	10q23.31	GI_34222091-S	-	n/s
-	*ISGF3 (IRF9)*	14q12	GI_25282406-S	-	n/s
-	*JAK1*	1p31.3	GI_4504802-S	-	n/s
-	*PML*	15q24.1	GI_15451762-I	-	n/s
-	PML	15q24.1	GI_15451776-A	-	n/s
-	*PRMT1 (HRMT1L2)*	19q13.33	GI_38195083	-	n/s
-	*PRMT1 (HRMT1L2)*	19q13.33	GI_38195086-A	-	n/s
-	*PTP-1B (PTPN1)*	20q13.13	GI_18104977-S	-	n/s
-	*SHP-1 (PTPN6)*	12p13.31	GI_34328901-A	-	n/s
-	*SHP-1 (PTPN6)*	12p13.31	GI_34328901-I	-	n/s
-	*SHP-1 (PTPN6)*	12p13.31	GI_34328902-I	-	n/s
-	*SHP-2 (PTPN11)*	12q24.13	GI_33356176-S	-	n/s
-	*SOCS1*	16p13.13	GI_4507232-S	-	n/s
-	*STAT1*	2q32.2	GI_21536299-I	-	n/s
-	*STAT1*	2q32.2	GI_21536300-A	-	n/s
-	*STAT1*	2q32.2	GI_21536300-I	-	n/s
AA 152 (0.72)	*STAT2*	12q13.3	GI_38202247-S	11.06±0.34	0.021[a]
AG 56 (0.27)	-	-	-	11.17±0.33	-
GG 2 (0.01)	-	-	-	11.57±0.38	-
-	*TYK2*	19p13.2	GI_34222294-S	-	n/s
-	*USP18*	22q11.21	GI_32313609-S	-	n/s

E, rs2295827 (C/T) with MS susceptible genes; Genetic Model, D; Genetic Factor, T

Genotype number (frequency)	Gene symbol	Chr. locus	Correlation between genotype and gene expression		
			Expression chip probe GI	Expression level (mean ± SD)	P-value
-	*CD6*	11q13	GI_5802993-S	-	n/s
-	*CD40 (TNFRSF5)*	20q13.12	GI_23312370-A	-	n/s
-	*CD58*	1p13.1	GI_4502676-S	-	n/s
CC 164 (0.78)	*HLA-A*	6p22.1	GI_24797066-S	12.08±1.58	0.036[a]
CT 44 (0.21)	-	-	-	11.46±1.76	-
TT 2 (0.01)	-	-	-	12.61±0.32	-
CC 164 (0.78)	*HLA-B*	6p21.33	GI_21327676-S	14.32±0.27	0.030[a]
CT 44 (0.21)	-	-	-	14.40±0.26	-
TT 2 (0.01)	-	-	-	14.65±0.56	-
-	*HLA-DRB*1	6p21.32	GI_4504410-S	-	n/s
-	*IL2RA*	10p15.1	GI_4557666-S	-	n/s
-	*IL7R*	5p13.2	GI_28610150-S	-	n/s
-	*IL12A*	3q25.33	GI_24430218-S	-	n/s
-	*IRF8 (ICSBP1)*	16q24.1	GI_4504566-S	-	n/s
-	*STAT3*	17q21.2	GI_21618337-A	-	n/s
-	*TNFRSF1A*	12p13.31	GI_23312372-S	-	n/s

Table SI. Continued.

F, rs2295827 (C/T) with IFN α/β signalling pathway genes; Genetic Model, D; Genetic Factor, T

Genotype number (frequency)	Gene symbol	Chr. locus	Correlation between genotype and gene expression		
			Expression chip probe GI	Expression level (mean ± SD)	P-value
-	IFI6 (G1P3)	1p36.11	GI_13259551-A	-	n/s
-	IFNA1	9p21.3	GI_13128949-S	-	n/s
-	IFNAR1	21q22.11	GI_10835182-S	-	n/s
-	IFNAR2	21q22.11	GI_19923128-S	-	n/s
-	IFNB1	9p21.3	GI_4504602-S	-	n/s
-	IRF1	5q31.1	GI_4504720-S	-	n/s
-	IRF2	4q35.1	GI_4755144-S	-	n/s
-	ISG15 (G1P2)	1p36.33	GI_4826773-S	-	n/s
-	ISG54 (IFIT2)	10q23.31	GI_34222091-S	-	n/s
-	ISGF3 (IRF9)	14q12	GI_25282406-S	-	n/s
-	JAK1	1p31.3	GI_4504802-S	-	n/s
-	PML	15q24.1	GI_15451762-I	-	n/s
-	PML	15q24.1	GI_15451776-A	-	n/s
-	PRMT1 (HRMT1L2)	19q13.33	GI_38195083	-	n/s
-	PRMT1 (HRMT1L2)	19q13.33	GI_38195086-A	-	n/s
-	PTP-1B (PTPN1)	20q13.13	GI_18104977-S	-	n/s
-	SHP-1 (PTPN6)	12p13.31	GI_34328901-A	-	n/s
-	SHP-1 (PTPN6)	12p13.31	GI_34328901-I	-	n/s
-	SHP-1 (PTPN6)	12p13.31	GI_34328902-I	-	n/s
-	SHP-2 (PTPN11)	12q24.13	GI_33356176-S	-	n/s
-	SOCS1	16p13.13	GI_4507232-S	-	n/s
-	STAT1	2q32.2	GI_21536299-I	-	n/s
-	STAT1	2q32.2	GI_21536300-A	-	n/s
-	STAT1	2q32.2	GI_21536300-I	-	n/s
-	STAT2	12q13.3	GI_38202247-S	-	n/s
-	TYK2	19p13.2	GI_34222294-S	-	n/s
-	USP18	22q11.21	GI_32313609-S	-	n/s

G, rs2348071 (G/A) with MS susceptible genes; Genetic Model, A; Genetic Factor, GA

Genotype number (frequency)	Gene symbol	Chr. locus	Correlation between genotype and gene expression		
			Expression chip probe GI	Expression level (mean ± SD)	P-value
-	CD6	11q12.2	GI_5802993-S	-	n/s
GG 76 (0.37)	CD58	1p13.1	GI_4502676-S	11.80±0.26	0.022[a]
GA 80 (0.38)	-	-	-	11.88±0.23	-
AA 52 (0.25)	-	-	-	11.90±0.23	-
-	HLA-A	6p22.1	GI_24797066-S	-	n/s
-	HLA-B	6p21.33	GI_21327676-S	-	n/s
-	HLA-DRB1	6p21.32	GI_4504410-S	-	n/s
-	IL2RA	10p15.1	GI_4557666-S	-	n/s
GG 76 (0.37)	IL7R	5p13.2	GI_28610150-S	6.31±0.22	0.0083[a]
GA 80 (0.38)	-	-	-	6.26±0.14	-
AA 52 (0.25)	-	-	-	6.22±0.20	-
-	IL12A	3q25.33	GI_24430218-S	-	n/s
-	IRF8 (ICSBP)	16q24.1	GI_4504566-S	-	n/s
GG 76 (0.37)	STAT3	17q21.2	GI_21618337-A	11.00±0.43	0.0001[a]
GA 80 (0.38)	-	-	-	11.09±0.35	-
AA 52 (0.25)	-	-	-	11.26±0.35	-
-	TNFRSF1A	12p13.31	GI_23312372-S	-	n/s
GG 76 (0.37)	TNFRSF5 (CD40)	20q13.12	GI_23312370-A	9.86±0.38	0.0033[a]

Table SI. Continued.

G, rs2348071 (G/A) with MS susceptible genes; Genetic Model, A; Genetic Factor, GA

Genotype number (frequency)	Gene symbol	Chr. locus	Correlation between genotype and gene expression		
			Expression chip probe GI	Expression level (mean ± SD)	P-value
GA 80 (0.38)	*TNFRSF5 (CD40)*	-	-	10.01±0.32	-
AA 52 (0.25)	*TNFRSF5 (CD40)*	-	-	10.05±0.37	-

G, rs2348071 (G/A) with IFN α/β signalling pathway genes; Genetic Model, A; Genetic Factor, GA

Genotype number (frequency)	Gene symbol	Chr. locus	Correlation between genotype and gene expression		
			Expression chip probe GI	Expression level (mean ± SD)	P-value
GG 76 (0.37)	*IFI6 (G1P3)*	1p36.11	GI_13259551-A	12.47±0.65	0.029[a]
GA 80 (0.38)	-	-	-	12.60±0.49	-
AA 52 (0.25)	-	-	-	12.69±0.48	-
-	*IFNA1 (IFN-alpha)*	9p21.3	GI_13128949-S	-	n/s
-	*IFNAR1*	21q22.11	GI_10835182-S	-	n/s
-	*IFNAR2*	21q22.11	GI_19923128-S	-	n/s
-	*IFNB1*	9p21.3	GI_4504602-S	-	n/s
-	*IRF1*	5q31.1	GI_4504720-S	-	n/s
GG 76 (0.37)	*IRF2*	4q35.1	GI_4755144-S	7.63±0.39	0.011[a]
GA 80 (0.38)	-	-	-	7.71±0.40	-
AA 52 (0.25)	-	-	-	7.81±0.36	-
-	*ISG15 (G1P2)*	1p36.33	GI_4826773-S	-	n/s
-	*ISG54 (IFIT2)*	10q23.31	GI_34222091-S	-	n/s
-	*ISGF3 (IRF9)*	14q12	GI_25282406-S	-	n/s
-	*JAK1*	1p31.3	GI_4504802-S	-	n/s
-	*PML (MYL)*	15q24.1	GI_15451762-I	-	n/s
-			GI_15451776-A	n/s	
GG 76 (0.37)	*PRMT1 (HRMT1L2)*	19q13.33	GI_38195083-I	6.96±0.15	0.017[a]
GA 80 (0.38)	*PRMT1 (HRMT1L2)*	19q13.33	GI_38195083-I	7.00±0.14	-
AA 52 (0.25)	*PRMT1 (HRMT1L2)*	19q13.33	GI_38195083-I	7.02±0.15	-
GG 76 (0.37)	*PRMT1 (HRMT1L2)*	19q13.33	GI_38195086-A	11.70±0.23	0.033[a]
GA 80 (0.38)	*PRMT1 (HRMT1L2)*	19q13.33	GI_38195086-A	11.80±0.24	-
AA 52 (0.25)	*PRMT1 (HRMT1L2)*	19q13.33	GI_38195086-A	11.78±0.21	-
GG 76 (0.37)	*PTP-1B (PTPN1)*	20q13.13	GI_18104977-S	11.03±0.28	0.0004[a]
GA 80 (0.38)	*PTP-1B (PTPN1)*	-	-	11.08±0.20	-
AA 52 (0.25)	*PTP-1B (PTPN1)*	-	-	11.18±0.21	-
-	*SHP-1 (PTPN6)*	12p13.31	GI_34328901-A	-	n/s
-	*SHP-1 (PTPN6)*	-	GI_34328901-I	-	n/s
-	*SHP-1 (PTPN6)*	-	GI_34328902-I	-	n/s
GG 76 (0.37)	*SHP-2 (PTPN11)*	12q24.13	GI_33356176-S	9.72±0.34	0.010[a]
GA 80 (0.38)	*SHP-2 (PTPN11)*	-	-	9.81±0.28	-
AA 52 (0.25)	*SHP-2 (PTPN11)*	-	-	9.86±0.24	-
-	*SOCS1*	16p13.13	GI_4507232-S	-	n/s
-	*STAT1*	2q32.2	GI_21536299-I	-	n/s
-			GI_21536300-A	n/s	
-			GI_21536300-I	n/s	
-	*STAT2*	12q13.3	GI_38202247-S	-	n/s
-	*TYK2*	19p13.2	GI_34222294-S	-	n/s
GG 76 (0.37)	*USP18*	22q11.21	GI_32313609-S	9.65±0.67	0.0004[a]
GA 80 (0.38)	-	-	-	9.95±0.47	-
AA 52 (0.25)	-	-	-	10.00±0.52	-

[a]Combine P-value of statistical analysis of all genotypes of SNP in the specific genetic model; genotype number (frequency) is given for HapMap unrelated subjects of CEU, YRI, HCB and JPT HapMap populations grouped in one HapMap unrelated subjects cohort. Expression level (mean ± SD) is indicated only if Spearman correlation (difference) is statistically significant. n/s, no statistically significant result.

Table SII. Summary on the genotype - phenotype correlation used in the genes whose expression levels in lymphoblastic cell lines are correlated with SNP genotype in the dominant model for the rs1048990, rs2295826 and rs2295827 and in the additive model for the rs2348071.

A, *MS susceptibility genes*

Gene symbol	Chr. location[a]	Protein encoded	GO annotation	Spearman correlation			
				rs1048990	rs2295826	rs2295827	rs2348071
CD58	1p13.1	Lymphocyte function-associated antigen 3	Signalling receptor binding	Yes	No	No	Yes
HLA-A	6p22.1	HLA class I histocompatibility antigen, A-2 alpha chain	Peptide antigen binding and receptor binding	Yes	No	No	No
HLA-B	6p22.1	HLA class I histocompatibilityantigen, B-51 alpha chain	Peptide antigen binding and receptor binding	No	Yes	Yes	No
IL7R	5p13.2	Interleukin-7 receptor subunit alpha	Antigen binding *and* interleukin-7 receptor activity.	Yes	No	No	Yes
STAT3	-	Signal Transducer And Activator Of Transcription 3	DNA-binding transcription factor activity and sequence-specific DNA binding.	Yes	No	No	Yes
TNFRSF5 (CD40)	20q13.12	Tumour necrosis factor receptor superfamily member 5	Identical protein binding and protein kinase activity.	Yes	No	No	Yes

B, *IFN α/β signalling pathway genes*

Gene symbol	Chr. location[a]	Protein encoded	GO annotation	Spearman correlation			
				rs1048990	rs2295826	rs2295827	rs2348071
IFI6 (G1P3)	1p35.3	Interferon Alpha Inducible Protein 6	Pro-apoptotic activity	No	No	No	Yes
IFNA1 (IFN α)	9p21.3	Interferon alpha 1/13	Cytokine activity *and* type I interferon receptor binding.	Yes	No	No	No
IRF1	5q31.1	Interferon regulatory factor 1	DNA-binding transcription factor activity *and* RNA polymerase II proximal promoter sequence-specific DNA binding.	Yes	No	No	No
IRF2	4q35.1	Interferon regulatory factor 2	DNA-binding transcription factor activity *and* DNA-binding transcription activator activity, RNA polymerase II-specific.	No	No	No	Yes
PRMT1 (HMRT1L2)	19q13.33	Protein arginine methyltransferase 1	Methyltransferase activity	No	No	No	Yes
PTP-1B (PTPN1)	20q13.13	Protein tyrosine phosphatase, non-receptor type 1	Enzyme binding.	Yes	No	No	Yes
SHP-2 (PTPN11)	12q24.13	Tyrosine-protein phosphatase non-receptor type 11	Protein domain specific binding *and* protein tyrosine phosphatase activity.	No	No	No	Yes

Table SII. Continued.

B, *IFN α/β signalling pathway genes*

Gene symbol	Chr. location[a]	Protein encoded	GO annotation	Spearman correlation			
				rs1048990	rs2295826	rs2295827	rs2348071
TYK2	19p13.2	Non-receptor tyrosine-protein kinase TYK2	Transferase activity, transferring phosphorus-containing groups *and* protein tyrosine kinase activity.	Yes	No	No	No
USP18	22q11.2	Ubl carboxyl-terminal hydrolase 18	Cysteine-type endopeptidase activity *and* thiol-dependent ubiquitinyl hydrolase activity.	Yes	No	No	Yes

[a]Cytogenetic band is given according to the Ensembl database; GO, gene ontology.

Table SIII. Spectrum and frequency of the 4 loci genotypes in patients with multiple sclerosis and healthy individuals and data on the association with disease.

ID	4 LG composition (L1-L2-L3-L4)	Frequency in the group (n %)		Association by frequency in additive model	
		MS (n=280)	Controls (n=305)	P-value	OR [95% CI]
4-LG1	CC-CC-AA-GG[a]	52 (18.57)	86 (28.19)	0.0312	0.66 [0.45-0.96]
4-LG2	CC-CC-AA-(GA+AA)	65 (23.21)	81 (26.56)	n/s	-
4-LG3	CC-CC-(AG+GG)-GG	18 (6.43)	24 (7.87)	n/s	-
4-LG4	CC-(CG+GG)-AA-GG	18 (6.43)	22 (7.21)	n/s	-
4-LG5	CC-(CG+GG)-AA-(GA+AA)	19 (6.79)	18 (5.90)	n/s	-
4-LG6	CA-CC-AA-(GA+AA)	16 (5.71)	18 (5.90)	n/s	-
4-LG7	CC-CC-(AG+GG)-(GA+AA)[b]	47 (16.79)	17 (5.57)	0.0001	3.01 [1.70-5.33]
4-LG8	CA-CC-AA-GG	17 (6.07)	16 (5.25)	n/s	-
4-LG9	CC-(CG+GG)-(AG+GG)-GG	5 (1.79)	8 (2.62)	-	-
4-LG10	CC-(CG+GG)-(AG+GG)-(GA+AA)	5 (1.79)	5 (1.64)	-	-
4-LG11	CA-CC-(AG+GG)-GG	8 (2.86)	4 (1.31)	-	-
4-LG12	CA-CC-(AG+GG)-(GA+AA)	10 (3.57)	4 (1.31)	-	-
4-LG13	CA-(CG+GG)-AA-GG	0 (0.00)	1 (0.33)	-	-
4-LG14	CA-(CG+GG)-AA-(GA+AA)	0 (0.00)	1 (0.33)	-	-

4 LG, 4 loci genotype; L1, L2, L3 and L4 indicate the rs2277460, rs1048990, rs2295826 and rs2348071 loci, respectively. The rs2295826 locus represents linkage block rs2295826 - rs2295827. [a]$P<0.05$, and [b]$P≤0.0001$. CI, confidence interval; OR, odds ratio; MS, multiple sclerosis; n/s, no statistical results; -, no statistical analysis made.

Table SIV. Allelic composition frequency of the 5 loci haplotypes in patients with multiple sclerosis and healthy individuals.

ID	1-2-3-4-5	Frequency in the group, [n (%)]		Association by frequency in additive model P-value	Association by frequency in additive model OR [95% CI]
		MS (n=560)	Control (n=610)		
Hap1	CCACG	258 (46.07)	311 (50.98)	n/s	-
Hap2	CCACA	108 (19.29)	142 (23.28)	n/s	-
Hap3	CCGTG	31 (5.54)	49 (8.03)	n/s	-
Hap4	CGACG	45 (8.04)	41 (6.72)	n/s	-
Hap5	ACACA	1 (0.18)	23 (3.77)	n/s	-
Hap6	ACACG[a]	47 (8.39)	21 (3.44)	0.00060	2.44 [1.45-4.11]
Hap7	CGGTG	0 (0.00)	13 (2.14)	-	-
Hap8	CCGTA[a]	62 (11.07)	7 (1.15)	<0.00010	9.65 [4.49-20.76]
Hap9	CGACA	5 (0.89)	3 (0.49)	n/s	-
Hap10	ACGTG	3 (0.54)	-	-	-

[a]At risk haplotypes; Hap, haplotype; L1, L2, L3, L4 and L5 indicate the rs2277460, rs1048990, rs2295826, rs2295827 and rs2348071 loci, respectively; MS, multiple sclerosis; n/s - no statistical results; -, no statistical analyse made; CI, confidence interval; OR, odds ratio.