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Supplementary Data

SORL1 is Genetically Associated with Neuropathologically Characterized Late-Onset Alzheimer's Disease

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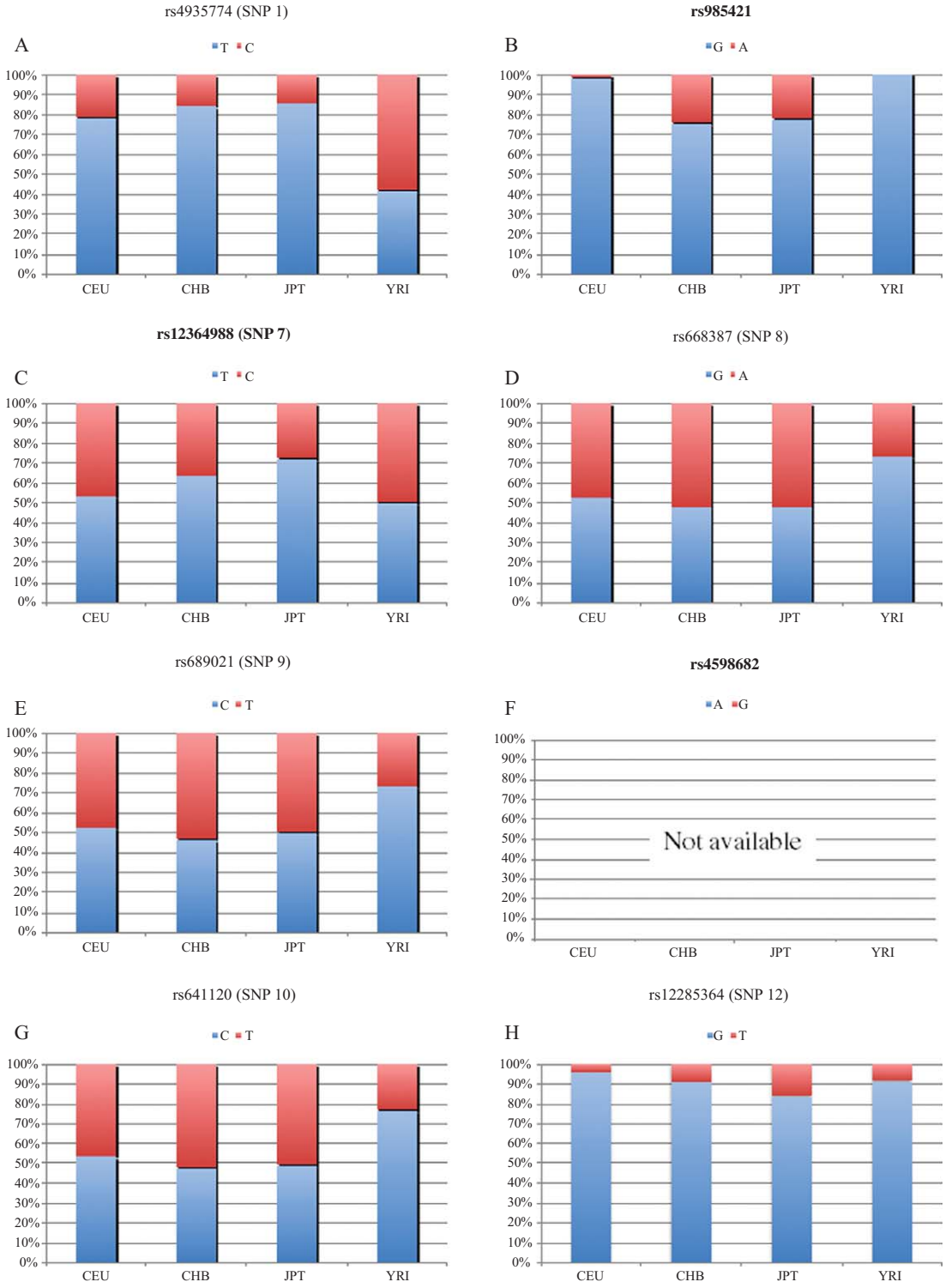
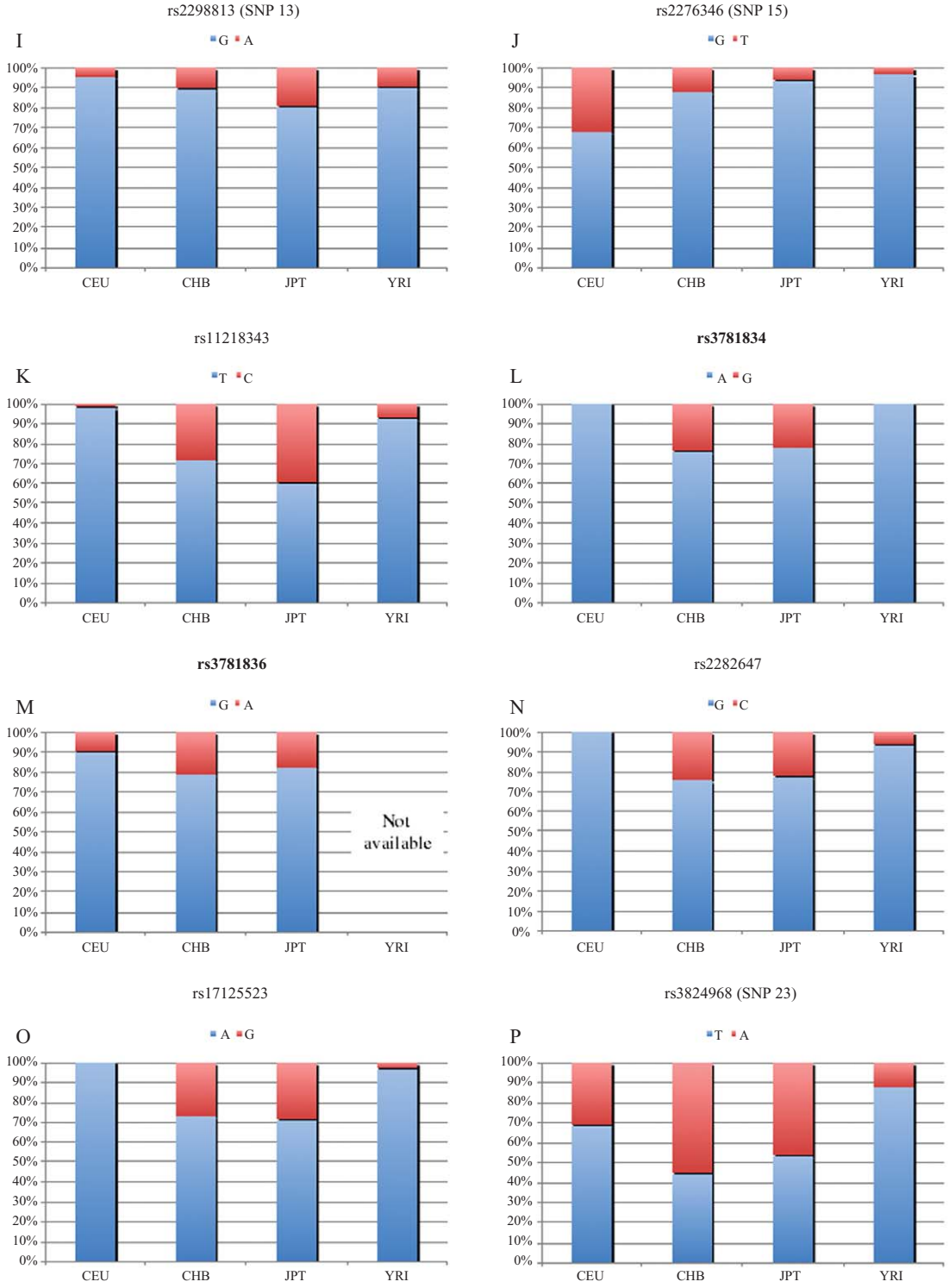
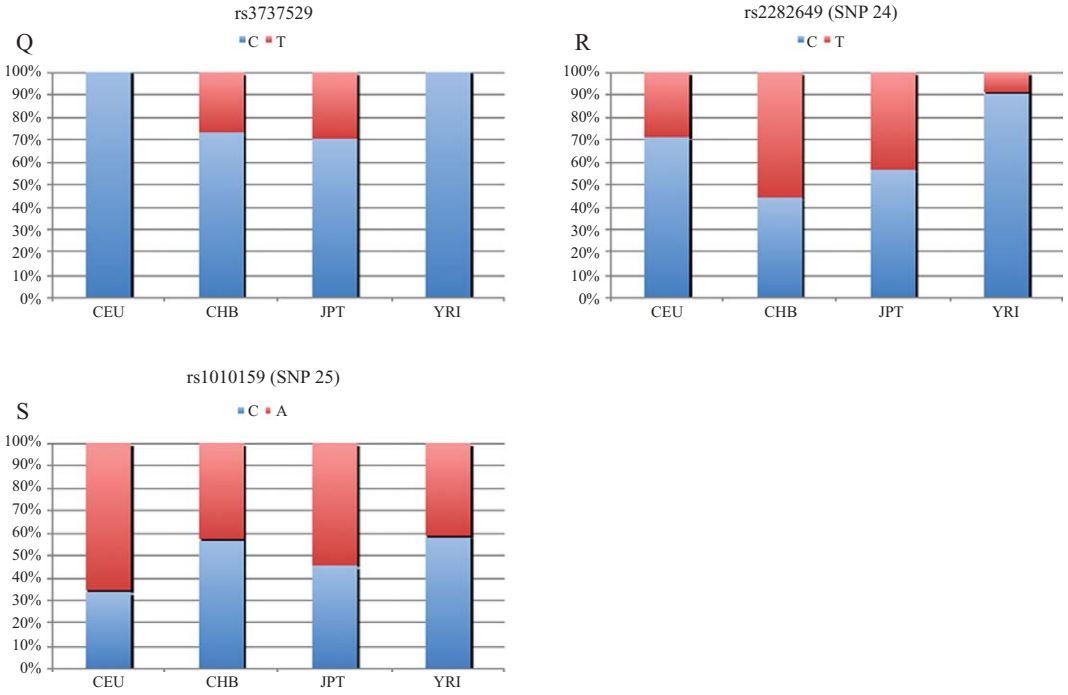


Supplementary Figure 1. Allelic frequency data from HapMap (Release #24) concerning the 19 SNPs examined in this study. The allelic frequencies for four populations, US Utah residents of northern and western European ancestry (CEU), Han Chinese in Beijing (CHB), Japanese in Tokyo (JPT), and Yoruba in Ibadan (YRI), Nigeria, are presented. Five significant SNPs, rs985421, rs12364988 (SNP 7), rs4598682, rs3781834, and rs3781836, found in a single SNP case-control study (Table 2 and Supplementary Table 2) are shown in boldface. Allelic frequency data for all four populations for SNP rs4598682 and those for YRI for SNP rs3781836 were not available in the HapMap database (Release #24).

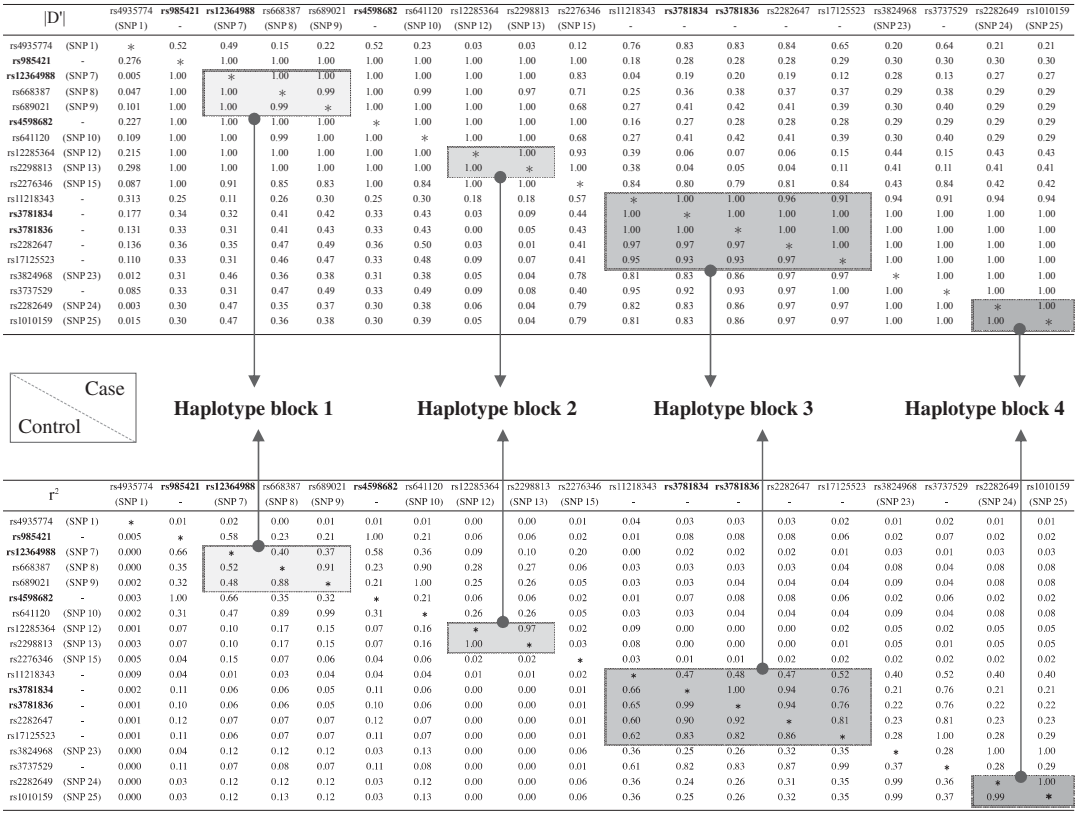


Supplementary Figure 1. (*Continued*)



Supplementary Figure 1. (*Continued*)

A

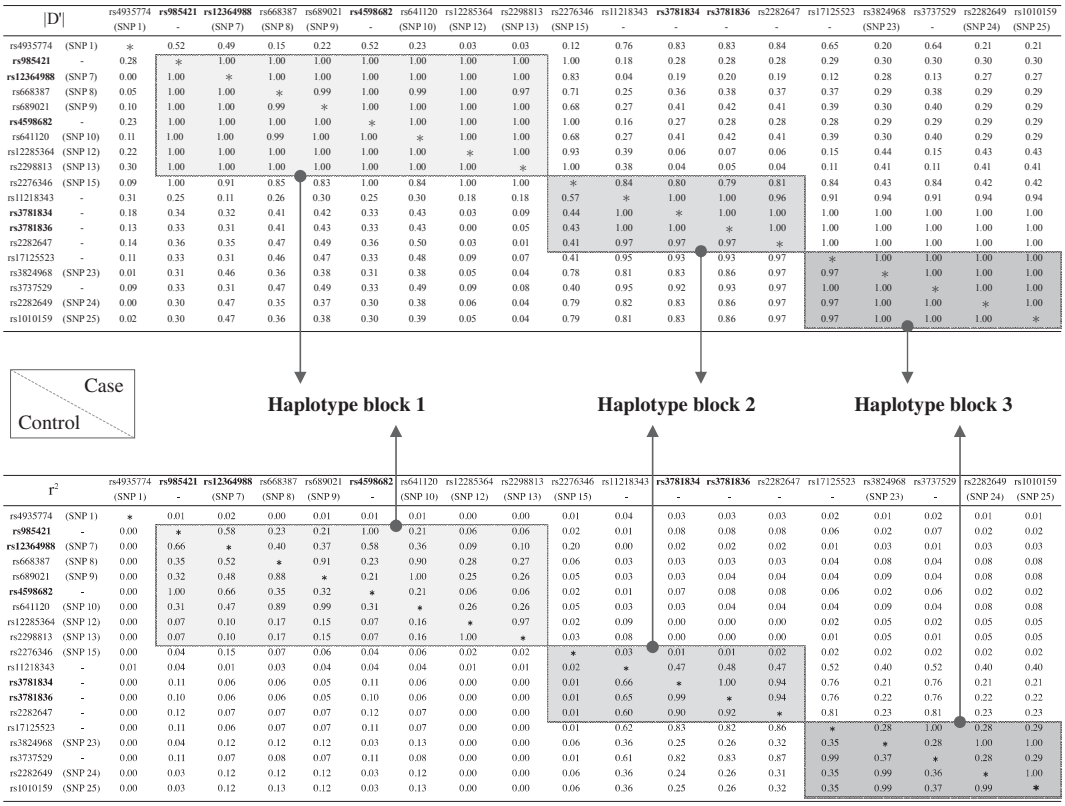


B

Haplotype block	Haplotype	Frequency		No. of estimated alleles		Permutation *P*	OR (95% CI)
		Cases	Controls	Cases	Controls	(10,000)	
1	M-m-m	0.499	0.459	213	340	2.05E-01	1.18 (0.93 - 1.49)
	m-M-M	0.268	0.358	114	265	**1.40E-03**	0.65 (0.50 - 0.85)
	M-M-M	0.211	0.156	90	115	**1.92E-02**	1.46 (1.07 - 1.98)
	M-m-M	0.022	0.028	9	20	6.92E-01	0.78 (0.35 - 1.72)
	Global *P*	-	-	-	-	**5.20E-03**	-
2	M-M	0.792	0.847	337	627	**1.63E-02**	0.68 (0.50 - 0.93)
	m-m	0.209	0.153	89	113	**1.63E-02**	1.47 (1.08 - 1.99)
	Global *P*	-	-	-	-	**1.63E-02**	-
3	M-M-M-M-M	0.689	0.655	294	484	2.18E-01	1.18 (0.91 - 1.52)
	m-m-m-m-m	0.177	0.254	75	188	**1.70E-03**	0.63 (0.47 - 0.85)
	m-M-M-M-M	0.107	0.077	46	57	8.34E-02	1.45 (0.96 - 2.18)
	m-M-M-M-m	0.027	0.014	11	11	1.85E-01	1.76 (0.75 - 4.09)
	Global *P*	-	-	-	-	**6.20E-03**	-
4	m-M	0.505	0.497	215	368	8.57E-01	1.03 (0.81 - 1.31)
	M-m	0.495	0.503	211	372	8.57E-01	0.97 (0.76 - 1.23)
	Global *P*	-	-	-	-	8.57E-01	-

Supplementary Figure 2. LD analysis. LD measures, |D'| and r^2, for the 19 *SORL1* SNPs examined were computed. Significant SNPs, i.e., rs985421, rs12364988 (SNP 7), rs4598682, rs3781834, and rs3781836, are depicted in boldface. The upper-right half shows AD cases and the lower-left half controls. Haplotype blocks were estimated using Gabriel et al.'s (A) and four gamete (C) methods [1], and are highlighted in grey-colored serial boxes. The results of the haplotype case-control study for each haplotype block are presented in B (Gabriel et al.'s method) and D (four gamete method). Permutation *p* (10,000 iterations of random sampling) of less than 0.05 are depicted in boldface. M, major allele; m, minor allele.

C



D

Haplotype block	Haplotype	Frequency		No. of estimated alleles		Permutation *P*	OR (95% CI)
		Cases	Controls	Cases	Controls	(10,000)	
1	M-M-m-m-M-m-M-M	0.500	0.459	213	340	1.99E-01	1.18 (0.93 - 1.49)
	m-m-M-M-m-M-M-M	0.176	0.269	75	199	**2.00E-04**	0.58 (0.43 - 0.78)
	M-M-M-M-M-M-m-m	0.212	0.154	90	114	**1.64E-02**	1.47 (1.08 - 2.00)
	M-m-M-M-M-M-M-M	0.094	0.090	40	67	8.35E-01	1.04 (0.69 - 1.57)
	M-M-m-M-M-M-M-M	0.019	0.027	8	20	4.25E-01	0.69 (0.30 - 1.58)
	Global *P*	-	-	-	-	**2.00E-03**	-
2	M-M-M-M-M	0.599	0.571	255	423	3.78E-01	1.12 (0.88 - 1.42)
	M-m-m-m-m	0.176	0.247	75	183	**5.40E-03**	0.65 (0.48 - 0.88)
	M-m-M-M-M	0.131	0.091	56	67	**2.74E-02**	1.52 (1.04 - 2.22)
	m-M-M-M-M	0.094	0.091	40	67	8.29E-01	1.04 (0.69 - 1.57)
	Global *P*	-	-	-	-	**1.17E-02**	-
3	M-M-M-m-M	0.505	0.495	215	366	7.63E-01	1.04 (0.82 - 1.32)
	m-m-m-M-m	0.218	0.271	93	200	5.17E-02	0.75 (0.57 - 1.00)
	M-m-M-M-m	0.277	0.235	118	174	1.23E-01	1.25 (0.95 - 1.64)
	Global *P*	-	-	-	-	8.92E-02	-

Supplementary Figure 2. (*Continued*)

Supplementary Table 1
SNP information

dbSNP	SNP No.[a]	Genomic position	SNP interval	SNP position	Allele				GSR	HWE *P*	
		(bp)[b]	(bp)		M	Frequency	m	Frequency		Cases	Controls
rs4935774	1	120,826,964	40,562	Upstream of 5' UTR	T	0.857 (0.86)	c	0.143 (0.14)	99.3%	0.2711	0.5136
rs985421	-	120,867,526	5,310	Intron 5	G	0.764 (0.78)	a	0.236 (0.22)	99.1%	0.8151	0.8952
rs12364988	7	120,872,836	295	Exon 6 (H269H)	T	0.674 (0.72)	c	0.326 (0.28)	99.3%	1.0000	0.7333
rs668387	8	120,873,131	3,199	Intron 6	C	0.502 (0.48)	t	0.498 (0.52)	99.7%	0.1327	0.4663
rs689021	9	120,876,330	4,831	Intron 6	G	0.525 (0.50)	a	0.475 (0.50)	98.1%	***0.0367***	0.9163
rs4598682	-	120,881,161	5,014	Intron 6	A	0.766 (N/A)	g	0.234 (N/A)	99.3%	0.8117	1.0000
rs641120	10	120,886,175	12,261	Intron 6	G	0.527 (0.49)	a	0.473 (0.51)	98.6%	0.0980	0.9160
rs12285364	12	120,898,436	458	Intron 9	C	0.829 (0.84)	t	0.171 (0.16)	99.7%	1.0000	0.6867
rs2298813	13	120,898,894	20,792	Exon 11 (T528A)	G	0.828 (0.80)	a	0.172 (0.20)	99.5%	1.0000	0.4186
rs2276346	15	120,919,686	21,111	Intron 13	G	0.907 (0.93)	t	0.093 (0.07)	99.5%	0.2271	0.1069
rs11218343	-	120,940,797	10,353	Intron 22	A	0.665 (0.60)	g	0.335 (0.40)	99.7%	0.7498	***0.0029***
rs3781834	-	120,951,150	2,398	Intron 24	A	0.771 (0.78)	g	0.229 (0.22)	99.5%	0.2250	0.1065
rs3781836	-	120,953,548	13,255	Intron 25	G	0.770 (0.82)	a	0.230 (0.18)	98.6%	0.2376	0.1367
rs2282647	-	120,966,803	12,646	Intron 30	C	0.772 (0.77)	g	0.228 (0.23)	98.8%	0.3520	0.1311
rs17125523	-	120,979,449	1,683	Intron 32	T	0.749 (0.71)	c	0.251 (0.29)	99.7%	0.4294	***0.0241***
rs3824968	23	120,981,132	1,894	Exon 34 (A1584A)	A	0.504 (0.47)	t	0.496 (0.53)	99.1%	0.7834	0.1431
rs3737529	-	120,983,026	1,142	Intron 36	G	0.750 (0.71)	a	0.250 (0.30)	99.7%	0.4294	***0.0246***
rs2282649	24	120,984,168	4,443	Intron 38	C	0.501 (0.57)	t	0.499 (0.43)	99.5%	0.8907	0.1441
rs1010159	25	120,988,611	-	Intron 39	C	0.501 (0.46)	t	0.499 (0.54)	99.3%	0.8907	0.2113

The allele frequency and genotyping success rate (GSR) of each SNP were computed by combining AD and control subjects: allele frequency values derived from HapMap JPT data (Release 24/Phase II on NCBI build 36) are shown in parentheses. HWE *p* of less than 0.05 are shown in boldface. M, major allele; m, minor allele; N/A, not available. [a]Rogaeva's SNP ID [2]. [b]According to NCBI build 36.

Supplementary Table 2
. Multiple logistic regression analysis of significant *SORL1* SNPs

dbSNP	SNP No.[a]	Allele		No. of subjects						Genotype: MM_{ref} vs Mm vs mm			
		M	m	Cases			Controls			Global *P*	OR_{MM} (ref.)	OR_{Mm} (95% CI)	OR_{mm} (95% CI)
				MM	Mm	mm	MM	Mm	mm				
rs985421	-	G	a	136	58	6	188	140	26	**0.009**	1.00	0.55 (0.36 - 0.84)**	0.39 (0.14 - 1.10)
rs12364988	7	T	c	106	80	14	142	168	44	**0.019**	1.00	0.64 (0.42 - 0.97)*	0.40 (0.19 - 0.85)*
rs4598682	-	A	g	136	58	6	188	140	26	**0.009**	1.00	0.55 (0.36 - 0.84)**	0.39 (0.14 - 1.10)
rs3781834	-	A	g	139	52	9	186	149	19	**0.001**	1.00	0.43 (0.27 - 0.67)***	0.49 (0.18 - 1.29)
rs3781836	-	G	a	139	52	9	188	147	19	**0.001**	1.00	0.44 (0.28 - 0.69)***	0.49 (0.19 - 1.31)

Global p of less than 0.05 are shown in boldface. M, major allele; m, minor allele; MM, major allele homozygote; Mm, heterozygote; mm, minor allele homozygote; ref, reference; $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$. [a]Rogaeva's SNP ID [2].

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