Supplementary Table 1. tSNPs, Primer Sequences, and Method of Genotyping

tSNP	Primer sequence	PCR program
rs3212657	F-TCCTGCCACCCAGTCAGT	Assay-by-Design
	FAM/VIC-ACATACAGACATAAGATG	
	R-GAAGAGAATGGGTTGGAGAGATAAGAAA	
rs1645761	F-CTCAAAACCACTGCTCCTTACATG	Assay-by-Design
	FAM/VIC-ATGTGAACCGTAAGTAA	
	R-AGACAATTCATTCAAGGGCTGCT	
rs3756541	F-GAGAAGTGGCTTGGAACAGGG	65TD55
	R-GCCACCATCTGGTAGACTTGCC	
rs1862639	F-CTGCCTCCCTCAAAGTCCTATT	65TD55
	R-CCTTGATAAACTGAGGTGCA	
	S1-CAGCTTCCTCCTTAGRG	
rs152088	F-GCTTTTGGCATCTTTATCATGAAATCCT	Assay-by-Design
	FAM/VIC-CCATTCCAAACATTG	
	R-GCAAAACCTGAAAGTATAAAACCTGGAA	
rs3212418	F-CAAGTTATCATACAGATATGAACAAGTTTATACAAGACT	Assay-by-Design
	FAM/VIC-CAATTCCATAGAACTCT	
	R-TTTCATCTCAGTAACTCAAATGGTCACA	
rs989073	F-GGAATAGCCTCTTGGTGATGT	65TD55
	R-AAGGCCTCGGTGAAATCC	
	S1-ATAGCCTCTTGGTGATG	

Supplementary Table 1 (continued)

tSNP	Primer sequence	PCR program
rs1363192	F-ACAATGATTGTTCTGATGTTATTTTTCAGTTGAG	Assay-by-Design
	FAM/VIC-CTAAGACAAATCACATGCC	
	R-CCACTGCCACATGTGAAAAACTAAA	
rs3212460	F-GCTCTGCAGCCTCACACATTAA	Assay-by-Design
	FAM/VIC-AACGCAATGCTTTC	
	R-GCATTGAATTTAGTGTCATCAATATAGGTACTTG	
rs3212476	F-CAGCGTTAGTGACTGCAGTTAATTG	Assay-by-Design
	FAM/VIC-CTTTGCCCACTTCC	
	R-CACAAATGAGGTTCACTGACTACCA	
rs984966	F-GTTGCTGACAATAAAGGGTTGTTCT	Assay-by-Design
	FAM/VIC-ATGGCTTTACCCCCC	
	R-ATTTTCTCAGTATTCTAAGTAAGTCTAAAGAGTTTAGTTTTT	
rs10513009	F-GGTGTCTTGGTAAGTGGGTAACA	Assay-by-Design
	FAM/VIC-CCTGTGAAATTTGT	
	R-TCTAAGTGTGAGTTAAAGTGATATCGACCT	
rs2303124	F-CCTTCAAGGGATTGTGGGACTATATC	Assay-by-Design
	FAM/VIC-CACTCTTTACCCTATCCAT	
	R-TGCTGATTATCTCCTGAGGCTATCT	

PCR, polymerase chain reaction; tSNP, haplotype-tagging single nucleotide polymorphism.

Supplementary Table 2. Demographic and Clinical Characteristics of SWISS Probands, ISGS Cases and Controls, and MSGD Cases and Controls*

Variable	Cases (*n*=484)	Controls (*n*=263)	*P* value
Age, mean±SD, y	65.6±14.2	60.0±14.7	<0.001
Female	226/484 (46.7)	163/263 (62.0)	<0.001
White	379/484 (78.3)	210/263 (79.8)	0.62
Risk factors			
Myocardial infarction	82/482 (17.0)	15/263 (5.7)	<0.001
AF	71/480 (14.8)	18/262 (6.9)	0.002
Chronic AF	35/480 (7.3)	10/262 (3.8)	0.06
Paroxysmal AF	40/478 (8.4)	9/262 (3.4)	0.01
Ever smoking	318/481 (66.1)	124/263 (47.1)	<0.001
Hypertension	335/482 (69.5)	101/260 (38.9)	<0.001
Hyperlipidemia†	215/433 (49.7)	56/211 (26.6)	<0.001
Diabetes mellitus	119/484 (24.6)	34/263 (12.9)	<0.001
Family history of stroke	252/481 (52.4)	88/263 (33.5)	<0.001

AF, atrial fibrillation; ISGS, Ischemic Stroke Genetics Study; MSGD, Mayo Stroke Genetics Databank; SWISS, Siblings With Ischemic Stroke Study.

*Values are presented as number (percentage) unless indicated otherwise.

†Missing in MSGD cohort.

Supplementary Table 3. tSNP Association Analysis (Adjusted for Age, Sex, Myocardial Infarction, Atrial Fibrillation, Smoking, Family History, and Diabetes Status) for Ischemic Stroke in White Patients

			No. of genotypes*			Association (*P* value)			
tSNP major/minor	Location	Group	11	12	22	General	Dominant	Additive	Recessive
rs3212657 T/C	52324239	Total	456	117	14	0.15	0.06	0.15	0.32
		Case	301	71	6				
		Control	155	46	8				
rs1645761 A/G	52332999	Total	442	135	11	0.18	0.32	0.06	0.08
		Case	293	81	5				
		Control	149	54	6				
rs3756541 C/T	52338852	Total	294	205	59	0.03	0.07	0.009	0.01
		Case	177	139	43				
		Control	117	66	16				
rs1862639 C/T	52343127	Total	373	193	22	0.65	0.36	0.56	0.75
		Case	243	125	11				
		Control	130	68	11				

Supplementary Table 3 (continued)

			No. of genotypes*			Association (*P* value)			
tSNP major/minor	Location	Group	11	12	22	General	Dominant	Additive	Recessive
rs152088 C/T	52344772	Total	403	160	22	0.56	0.38	0.31	0.40
		Case	267	100	11				
		Control	136	60	11				
rs3212418 T/C	52351929	Total	195	271	116	0.34	0.28	0.14	0.18
		Case	136	172	67				
		Control	59	99	49				
rs989073 C/A	52369177	Total	257	237	70	0.54	0.32	0.70	0.89
		Case	169	152	45				
		Control	88	85	25				
rs1363192 A/C	52373840	Total	294	243	50	0.14	0.09	0.63	0.70
		Case	186	169	24				
		Control	108	74	26				

Supplementary Table 3 (continued)

			No. of genotypes*			Association (*P* value)			
tSNP major/minor	Location	Group	11	12	22	General	Dominant	Additive	Recessive
rs3212460 C/T	52376431	Total	544	23	21	0.29	0.12	0.19	0.34
		Case	349	15	15				
		Control	195	8	6				
rs3212476 C/G	52379113	Total	325	220	41	0.31	0.96	0.24	0.14
		Case	216	137	25				
		Control	109	83	16				
rs984966 T/A	52404679	Total	201	288	98	0.95	0.86	0.76	0.76
		Case	131	187	60				
		Control	70	101	38				
rs10513009 C/T	52407631	Total	487	94	7	0.18	0.07	0.19	0.36
		Case	314	63	2				
		Control	173	31	5				

Supplementary Table 3 (continued)

			No. of genotypes*			Association (*P* value)			
tSNP major/minor	Location	Group	11	12	22	General	Dominant	Additive	Recessive
rs2303124 C/T	52414713	Total	235	221	112	0.08	0.55	0.08	0.03
		Case	142	150	75				
		Control	93	71	37				

tSNP, haplotype-tagging single nucleotide polymorphism.

*Genotype 11 indicates the presence of both major alleles; genotype 12, 1 major allele and 1 minor allele; and genotype 22, both minor alleles.

Supplementary Table 4. tSNP Association Analysis (Adjusted for Age, Sex, Myocardial Infarction, Atrial Fibrillation, Smoking, Family History, and Diabetes Status) for Ischemic Stroke in Nonwhite Patients

			No. of genotypes*			Association (*P* value)			
tSNP major/minor	Location	Group	11	12	22	General	Dominant	Additive	Recessive
rs3212657 T/C	52324239	Total	139	18	0	…	…	0.71	0.71
		Case	94	11	0				
		Control	45	7	0				
rs1645761 A/G	52332999	Total	76	63	19	0.21	0.08	0.11	0.28
		Case	53	42	10				
		Control	23	21	9				
rs3756541 C/T	52338852	Total	115	32	3	<0.001	…	0.02	0.02
		Case	70	25	3				
		Control	45	7	0				
rs1862639 C/T	52343127	Total	90	59	8	0.34	0.31	0.14	0.19
		Case	63	37	4				
		Control	27	22	4				

Supplementary Table 4 (continued)

			No. of genotypes*			Association (*P* value)			
tSNP major/minor	Location	Group	11	12	22	General	Dominant	Additive	Recessive
rs152088 C/T	52344772	Total	96	50	12	0.61	0.39	0.35	0.46
		Case	68	31	6				
		Control	28	19	6				
rs3212418 T/C	52351929	Total	18	72	68	0.13	0.04	0.08	0.60
		Case	14	52	39				
		Control	4	20	29				
rs989073 C/A	52369177	Total	71	69	15	0.47	0.24	0.28	0.48
		Case	48	47	8				
		Control	23	22	7				
rs1363192 A/C	52373840	Total	86	56	16	0.35	0.22	0.16	0.24
		Case	59	38	8				
		Control	27	18	8				

Supplementary Table 4 (continued)

			No. of genotypes*			Association (*P* value)			
tSNP major/minor	Location	Group	11	12	22	General	Dominant	Additive	Recessive
rs3212460 C/T	52376431	Total	143	10	5	0.63	0.64	0.39	0.34
		Case	93	8	4				
		Control	50	2	1				
rs3212476 C/G	52379113	Total	54	82	22	0.42	0.50	0.77	0.37
		Case	35	57	13				
		Control	19	25	9				
rs984966 T/A	52404679	Total	73	67	18	0.78	0.48	0.64	0.85
		Case	49	45	11				
		Control	24	22	7				
rs10513009 C/T	52407631	Total	113	38	6	0.33	0.24	0.98	0.61
		Case	72	29	3				
		Control	41	9	3				

Supplementary Table 4 (continued)

			No. of genotypes*			Association (*P* value)			
tSNP major/minor	Location	Group	11	12	22	General	Dominant	Additive	Recessive
rs2303124 C/T	52414713	Total	124	24	2	0.06	0.08	0.44	0.20
		Case	80	19	1				
		Control	44	5	1				

tSNP, haplotype-tagging single nucleotide polymorphism.

*Genotype 11 indicates the presence of both major alleles; genotype 12, 1 major allele and 1 minor allele; and genotype 22, both minor alleles.

Supplementary Table 5. tSNP Association (Unadjusted Analysis) and Haplotype Structure in White Patients*

		White				Haplotype marker				
tSNP name	tSNP no.	2 df	Dom	Add	Rec	1	2	3	4	5
rs3212657	1	0.13	0.13	0.06	0.09	0.06	0.17	0.11	0.18	0.28
rs1645761	2	0.17	0.11	0.07	0.18	0.07	0.03	0.09	0.24	0.44
rs3756541†	3	0.08	0.03	0.02	0.15	0.02	0.09	0.21	0.30	0.45
rs1862639	4	0.35	0.64	0.38	0.15	0.38	0.20	0.31	0.28	0.29
rs152088	5	0.24	0.22	0.12	0.14	0.12	0.09	0.06	0.13	0.10
rs3212418	6	0.09	0.06	0.03	0.09	0.03	0.01	0.10	0.12	0.17
rs989073	7	0.92	0.70	0.73	0.91	0.73	0.80	0.28	0.23	0.45
rs1363192	8	0.01	0.51	0.55	0.01	0.55	0.05	0.06	0.13	0.22
rs3212460†	9	0.79	0.59	0.52	0.50	0.40	0.48	0.15	0.12	0.09
rs3212476	10	0.54	0.27	0.28	0.62	0.28	0.42	0.16	0.66	…
rs984966	11	0.77	0.78	0.56	0.47	0.56	0.68	0.50	…	…
rs10513009	12	0.13	0.94	0.55	0.05	0.58	0.36	…	…	…
rs2303124†	13	0.21	0.08	0.14	0.56	0.11	…	…	…	…

Supplementary Table 5 (continued)

Add, additive; df, degrees of freedom; Dom, dominant; Rec, recessive; tSNP, haplotype-tagging single nucleotide polymorphism.

*tSNPs listed in order of position on the physical map. Haplotype data are reported as empiric *P* values.

†Not in Hardy-Weinberg equilibrium.

Supplementary Table 6. tSNP Association (Unadjusted Analysis) and Haplotype Structure in Nonwhite Patients*

		Nonwhite				Haplotype marker				
tSNP name	tSNP no.	2 df	Dom	Add	Rec	1	2	3	4	5
rs3212657	1	0.78	0.51	0.49	0.72	0.60	0.04	0.02	0.004	0.004
rs1645761	2	0.37	0.40	0.21	0.17	0.19	0.06	0.02	0.006	0.02
rs3756541†	3	0.14	0.05	0.05	0.34	0.02	0.06	0.02	0.05	0.30
rs1862639	4	0.38	0.24	0.17	0.30	0.19	0.04	0.08	0.18	0.20
rs152088	5	0.26	0.15	0.10	0.21	0.09	0.08	0.15	0.08	0.10
rs3212418	6	0.10	0.04	0.04	0.28	0.04	0.06	0.02	0.06	0.16
rs989073	7	0.53	0.78	0.47	0.26	0.47	0.13	0.26	0.40	0.09
rs1363192	8	0.34	0.53	0.26	0.14	0.24	0.19	0.45	0.12	0.40
rs3212460†	9	0.63	0.34	0.39	0.64	0.17	0.44	0.47	0.91	0.65
rs3212476	10	0.62	0.75	0.85	0.43	0.86	0.63	0.87	0.49	…
rs984966	11	0.88	0.87	0.72	0.61	0.71	0.82	0.43	…	…
rs10513009	12	0.26	0.32	0.64	0.36	0.54	0.24	…	…	…
rs2303124†	13	0.35	0.28	0.46	0.54	0.32	…	…	…	…

Supplementary Table 6 (continued)

Add, additive; df, degrees of freedom; Dom, dominant; Rec, recessive; tSNP, haplotype-tagging single nucleotide polymorphism.

*tSNPs listed in order of position on the physical map. Haplotype data are reported as empiric *P* values.

†Not in Hardy-Weinberg equilibrium.

Supplementary Table 7. Significant Haplotypes Based on 2-, 3-, 4-, 5-tSNP Window Analyses Including/Excluding tSNPs not in Hardy-Weinberg Equlibrium (Overall Data)

		Haplotype marker			
		2	3	4	5
		P value	*P* value	*P* value	*P* value
tSNP name	tSNP no.	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Analysis including tSNPs not in the Hardy-Weinberg equilibrium					
rs3212657	1	C.G	T.A.T	T.A.T.C	…
		0.04	0.04	0.03	
		0.58 (0.40-0.84)	1.47 (1.14-1.89)	1.49 (1.15-1.94)	
rs1645761	2	A.T	A.T.C	…	A.T.C.C.T
		0.04	0.04		0.04
		1.45 (1.12-1.87)	1.45 (1.12-1.88)		1.46 (1.12-1.89)
rs3756541*	3	T.C	T.C.C	T.C.C.T	…
		0.03	0.05	0.04	
		1.49 (1.15-1.93)	1.43 (1.10-1.85)	1.47 (1.13-1.91)	

Supplementary Table 7 (continued)

		Haplotype marker			
		2	3	4	5
		P value	*P* value	*P* value	*P* value
tSNP name	tSNP no.	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
rs1862639	4	C.C 0.06 1.35 (1.09-1.67)	…	…	…
rs152088	5	C.T 0.06 1.34 (1.08-1.66)	…	…	…
rs3212418	6	…	…	…	…
rs3212460*	9	…	…	…	C.C.T.C.T 0.02 1.60 (1.22-2.11)

Supplementary Table 7 (continued)

		Haplotype marker			
		2	3	4	5
		P value	*P* value	*P* value	*P* value
tSNP name	tSNP no.	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
rs3212476	10	…	…	C.T.C.T	…
				0.03	
				1.54 (1.17-2.02)	
rs984966	11	…	…	…	…
rs10513009	12	…	…	…	…
rs2303124*	13	…	…	…	…
Analysis excluding tSNPs not in Hardy-Weinberg equilibrium					
rs321657	1	C.G	C.G.C	…	…
		0.04	0.04		
		0.58 (0.40-0.84)	0.58 (0.40-0.84)		

Supplementary Table 7 (continued)

		Haplotype marker			
		2	3	4	5
		P value	*P* value	*P* value	*P* value
tSNP name	tSNP no.	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
rs1645761	2	A.C	A.C.C	…	…
		0.05	0.04		
		1.36 (1.09-1.69)	1.36 (1.10-1.68)		
rs1862639	4	C.C	…	…	…
		0.06			
		1.35 (1.09-1.67)			
rs152088	5	C.T	…	…	…
		0.06			
		1.34 (1.08-1.66)			

CI, confidence interval; OR, odds ratio; tSNP, haplotype-tagging single nucleotide polymorphism.

*Not in Hardy-Weinberg equilibrium.

Supplementary Table 8. Significant Haplotypes Based on 2-, 3-, 4-, 5-tSNP Window Analyses Including tSNPs not in Hardy-Weinberg Equilibrium (White Group)*

		Haplotype marker			
		2	3	4	5
		P value	*P* value	*P* value	*P* value
tSNP name	tSNP no.	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
rs3212657	1	…	T.A.T	T.A.T.C	…
			0.05	0.04	
			1.47 (1.11-1.93)	1.49 (1.13-1.96)	
rs1645761	2	…	A.T.C	…	A.T.C.C.T
			0.06		0.06
			1.45 (1.10-1.91)		1.46 (1.11-1.93)
rs3756541†	3	…	…	C.T.T.C	…
				0.06	
				1.47 (1.11-1.94)	
rs1862639	4	…	…	…	…
rs152088	5	…	…	…	…

Supplementary Table 8 (continued)

		Haplotype marker			
		2	3	4	5
		P value	*P* value	*P* value	*P* value
tSNP name	tSNP no.	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
rs3212418	6	…	…	…	…
rs989073	7	…	…	…	…
rs1363192	8	…	…	…	…
rs3212460†	9	…	…	…	C.C.T.C.T 0.02 1.65 (1.23-2.21)
rs3212476	10	…	…	C.T.C.T 0.04 1.52 (1.15-2.03)	…
rs984966	11	…	…	…	…
rs10513009	12	…	…	…	…
rs2303124†	13	…	…	…	…

Supplementary Table 8 (continued)

CI, confidence interval; OR, odds ratio; tSNP, haplotype-tagging single nucleotide polymorphism.

*No significant results excluding tSNPs not in Hardy-Weinberg equilibrium.

†Not in Hardy-Weinberg equilibrium.

Supplementary Table 9. Significant Haplotypes Based on 2-, 3-, 4-, 5-tSNP Window Analyses Excluding tSNPs not in Hardy-Weinberg Equilibrium (Nonwhite Patients)*

		Haplotype marker			
		2	3	4	5
		P value	*P* value	*P* value	*P* value
tSNP name	tSNP no.	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
rs3212657	1	…	…	T.A.C.C	T.A.C.C.T
				0.03	0.03
				2.52 (1.34-4.74)	2.62 (1.37-5.00)
rs1645761	2	A.C	A.C.C	A.C.C.T	…
		0.06	0.04	0.04	
		1.91 (1.18-3.09)	3.02 (1.61-5.67)	2.51 (1.32-4.78)	
rs1862639	4	…	…	…	…
rs152088	5	…	…	…	…
rs3212418	6	…	…	…	…

CI, confidence interval; OR, odds ratio; tSNP, haplotype-tagging single nucleotide polymorphism.

*No significant results involving tSNPs not in Hardy-Weinberg equilibrium.