SUPPLEMENTAL MATERIAL

Supplementary Methods.

Discovery population: The University of Maryland's Genetics of Early Onset Stroke (UMD-GEOS) Study is a population-based case-control study designed to identify genes associated with early-onset ischemic stroke and to characterize interactions of identified stroke genes and/or single nucleotide polymorphisms (SNPs) with environmental risk factors. Participants include men and women aged 18-49 from Baltimore-Washington, DC area, primarily of European-American (EA) and African-American (AA) ancestry and has been previously described[3] (see **Supplementary Table I**). In brief, incident ischemic stroke cases were matched to population-based controls free of stroke by age, ethnicity, gender, and geographic region. All subjects were interviewed for medical history and vascular risk factors; DNA was obtained from all subjects. All UMD-GEOS cases were subtyped by TOAST[4]. After exclusions, study subjects underwent genotyping on Illumina Human Exome Bead Chip v1.2 at the University of Texas-Houston (UT-H). Genotyping statistics included a SNP pass rate of 99.48% (successful-loci (n=243,497)/attempted-loci (n=244,770)) with 32,933 SNPs manually corrected. zCall_v3.4_GenomeStudio[10] was used to determine genotypes for any missing calls. Samples were removed if ancestry matched controls were unavailable or had cryptic relatedness to other study participants resulting in 723 cases and 726 controls.

Power: Here we discuss the Discovery population power for both single variant analysis and aggregate gene-based analysis. Based upon sample size limitations, this exome-chip association study was primarily designed to identify those exome variants, that when aggregated together within the corresponding gene, would exhibit significant association with stroke outcome.

First, for SINGLE variant association analysis with the 723 cases and 726 controls in our study, we have 80% power to detect associated low frequency and rare exome variants with minor allele frequency (MAF) less than 1% and effect size OR larger than 5 at exome-wide significance (p<2.05E-7), and 80% power to detect associated common exome variants with minor allele frequency (MAF) between 5-50% and effect size OR between 1.8~2.5 at exome-wide significance (p<2.05E-7). Our current study does not have sufficient power for exome variants (MAF<1%) with low or rare frequency, as well as smaller effect size OR<5. For those with effect size OR at least 3, a similar study would need at least 1880 cases and 1880 controls to detect the association at 80% power; for those with effect size OR at least 2, we would need at least 5550 case and 5550 control to achieve 80% power.

As described in the manuscript, GENE-based burden-testing evaluated for the association between all-stroke and TOAST-subtypes as outcomes with each gene. Only genes with two or more SNPs were included and with these genes further filtered to include those with a cumulative minor-allele-count >/=20 across all SNPs. To assess power, we carried out power simulations using the R SKAT package[5] and based on a simulated dataset in SKAT containing 200kb region with 10,000 haplotypes. The power is estimated as percent of SKAT-O tests on the 100 simulations reaching a Bonferroni corrected alpha level 0.05/10,518=4.75E-6 for multiple testing on 10,518 candidate genes (as consistent with our small vessel results). Assuming the percentage of casual rare SNPs within a gene being 30% or larger and with 723 ischemic stroke cases and 726 controls, we have >80% power to detect an associated gene with 25kb or longer length and the effect size of the underlying SNPs (odds ratio, OR) larger than 2.0. With 123 small vessel strokes and 726 controls, we have >80% power to detect an associated gene with 40kb or longer length and the effect size of the underlying causal SNPs (odds ratio, OR) larger than 2.5. As a reference, we found that *NAT10* was significantly associated with small vessel stroke at exome wide significance, which has a gene length of 45.47kb.

Genetic replication and extension to older-onset stroke: Replication of the top-associated SNPs and genes identified in UMD-GEOS was sought in two other datasets including: 1) an independent set of early-onset-stroke studies from the Genetics-of-Early-Onset-Stroke-Consortium as previously described by Cheng *et al.*[3] ; 2) a large-scale genome-wide-association-study of primarily older-onset-stroke, MEGASTROKE.[7] First, we excluded the GEOS samples from the Cheng *et al*. meta-analysis (resulting in 3,676 cases and 21,118 controls) and re-meta-analyzed the data. Additionally, we surveyed summary results from the large predominately older-onset stroke study MEGASTROKE (67,162 cases and 454,450 controls) that included GEOS samples as a very small subset.

Supplementary Table I. Characteristics of the UM-GEOS study by case-control status.

	Cases	**Controls**	**P-value***
Samples with Exome Chip (and prior GWAS)	723	726	
Age (mean +- SD, years)	39.8+6.8	41.9 + 6.7	<0.001
Female (%)	37.3	39.7	0.363
Self-reported race			0.078
African ancestry (n= 628)	330	298	
European Ancestry (n=821)	393	428	
Stroke Subtype n (%)			
Cardioembolic	141 (19.4)	-	-
Large-Artery	52 (7.2)	-	-
Lacunar/Small-Vessel	123 (16.9)	-	-
Other Known Causes	39 (5.4)	-	-
Undetermined Causes	368 (50.7)	-	-
Hypertension (%)	21.8	10.2	<0.001
Diabetes mellitus (%)	8.8	2.4	<0.001
Angina/ MI (%)	0.3	2.8	0.38
Current Smokers (%)	22.2	14.2	<0.001

*Unadjusted p-values for age and sex; other variables adjusted for age and sex.

Supplementary Table II. Single-variant Ancestry-specific Results for All-Stroke and Subtypes.

Population	Chr	BP	SNP	Gene	EA*	EAF**	OR	SE	L95	U95	P
All-Stroke											
European-American	4	184612553	rs67383011	*TRAPC11*	C	0.09	0.43	0.183	0.30	0.62	5.19E-06
	15	59981515	rs3087328	*BNIP2*	G	0.42	1.54	0.105	1.25	1.89	3.42E-05
	15	59981590	rs754641	*BNIP2*	A	0.43	1.54	0.104	1.25	1.89	3.42E-05
	9	100696203	rs755109	*HEMGN*	C	0.37	1.54	0.107	1.24	1.89	5.91E-05
	9	100684757	rs3183927	*TRMO*	G	0.37	1.52	0.106	1.23	1.87	8.96E-05
African-American	1	55304970	rs7549251	*LEXM*	G	0.61	1.65	0.118	1.30	2.08	2.35E-05
	11	6790028	rs10839616	*OR2AG2*	G	0.33	1.71	0.133	1.31	2.22	5.52E-05
	1	165702346	rs12723198	*TMCO1*	C	0.47	1.59	0.121	1.25	2.02	1.31E-04
	5	178381722	rs57272473	*ZNF454*	T	0.58	1.55	0.117	1.23	1.94	1.73E-04
	5	89989802	rs111033430	*GPR98*	G	0.067	2.67	0.264	1.59	4.48	1.91E-04
Cardio-embolic											
European-American	2	179569387	rs72650006	*TTN*	A	0.02	6.012	0.4289	2.594	13.94	2.88E-05
	19	53612055	rs10410030	*ZNF415*	C	0.17	2.474	0.225	1.592	3.845	5.68E-05
	1	248496863	rs4481887	*OR2M7*	A	0.26	2.096	0.1956	1.429	3.075	0.000155
	14	20444012	rs3861512	*OR4K15*	T	0.23	2.056	0.1958	1.401	3.018	0.000231
	10	14974905	rs12768894	*DCLRE1C*	C	0.17	2.207	0.2152	1.448	3.365	0.000235
African-American	12	10342736	rs78737759	*TMEM52B*	A	0.05	4.673	0.3636	2.291	9.531	2.23E-05
	17	72691928	rs2034310	*CD300LF*	T	0.38	0.373	0.2436	0.2312	0.6007	5.07E-05
	13	36122567	rs4606576	*MIR548F5*	C	0.28	0.461	0.2067	0.3071	0.6906	0.000176
	16	81010073	rs1127390	*CMC2*	T	0.40	0.447	0.22	0.2905	0.6883	0.000255
	1	173915909	rs61741479	*RC3H1*	C	0.04	3.965	0.3799	1.883	8.349	0.000288
Small-Vessel											
European-American	18	46645157	rs138427861	*DYM*	T	0.004	58.72	1.039	7.664	449.8	8.84E-05
	3	180104190	rs7612449	*TTC14*	T	0.022	11.19	0.6188	3.328	37.64	9.50E-05
	15	41488231	rs139947718	*EXD1*	C	0.005	69.58	1.109	7.919	611.4	0.000130
	13	103513944	rs1047769	*BIVM* *ERCC5*	G	0.04	6.161	0.4808	2.401	15.81	0.000156
	16	58752137	rs139235307	*GOT2*	T	0.02	10.18	0.6179	3.032	34.17	0.000173
African-American	20	31024013	rs75887545	*ASXL1*	G	0.024	21.19	0.7233	5.135	87.47	2.42E-05
	1	55317935	rs11555496	*DHCR24*	T	0.03	8.922	0.5552	3.005	26.49	8.09E-05
	19	33698291	rs3745974	*LRP3*	T	0.35	0.377	0.2551	0.2284	0.6209	0.000129
	1	117617973	rs34334470	*TTF2*	G	0.02	12.46	0.6645	3.388	45.83	0.000147
	17	46053353	rs12948207	*CDK5RAP3*	A	0.08	3.614	0.3489	1.824	7.161	0.000231
Large-Artery											
European-American	15	81578139	rs4072111	*IL16*	T	0.12	5.406	0.3958	2.489	11.74	2.01E-05
	2	85590286	rs7564372	*ELMOD3*	T	0.02	38.21	0.8685	6.965	209.7	2.73E-05
	2	189918622	rs116298748	*COL5A2*	A	0.02	9.293	0.5757	3.007	28.72	0.000108
	2	189931144	rs35852101	*COL5A2*	G	0.02	9.293	0.5757	3.007	28.72	0.000108
	15	98490612	rs4965115	*ARRDC4*	T	0.22	3.154	0.3006	1.75	5.686	0.000133
African-American	4	3494898	rs6850908	*DOK7*	T	0.06	16.31	0.5801	5.233	50.85	1.49E-06
	4	3494600	rs6811423	*DOK7*	G	0.06	15.91	0.6019	4.891	51.78	4.28E-06
	21	35186290	rs147036952	*ITSN1*	A	0.01	57.66	0.9286	9.342	355.8	1.26E-05

	21	34889697	rs34588874	*GART*	C	0.02	19.32	0.6928	4.969	75.1	1.92E-05
	19	33356891	rs12460876	*SLC7A9*	C	0.28	5.499	0.4132	2.447	12.36	3.69E-05
Other Known											
European-American	2	43902763	rs148112877	*LOC728819*	C	0.016	17.87	0.6763	4.748	67.27	2.01E-05
	19	50720949	rs34773557	*MYH14*	A	0.007	38.25	0.8711	6.936	210.9	2.88E-05
	2	99005601	rs6743554	*CNGA3*	C	0.36	4.497	0.36	2.22	9.107	2.98E-05
	5	140774689	rs72790033	*PCDHGA8*	C	0.36	7.026	0.5029	2.622	18.83	0.000106
	16	11272287	rs72650688	*CLEC16A*	A	0.004	99.03	1.187	9.67	1014	0.000108
African-American	20	20071521	rs111472581	*CFAP61*	A	0.02	20.18	0.7122	4.997	81.49	2.45E-05
	6	43519174	rs61739889	*XPO5*	C	0.02	22.1	0.7404	5.179	94.34	2.90E-05
	14	71514668	rs78161372	*PCNX*	C	0.01	48.17	0.9541	7.425	312.6	4.88E-05
	8	120007420	rs2062377	*COLEC10*	A	0.14	7.419	0.505	2.757	19.96	7.25E-05
	3	38101245	rs34012183	*DLEC1*	T	0.05	10.17	0.5924	3.186	32.49	8.99E-05
Undetermined											
European-American	20	6093177	rs16991866	*FERMT1*	G	0.12	2.212	0.1829	1.546	3.166	1.43E-05
	20	6088265	rs62200482	*FERMT1*	A	0.11	2.24	0.1862	1.555	3.226	1.48E-05
	4	184612553	rs67383011	*TRAPPC11*	C	0.10	0.338	0.2534	0.2056	0.555	1.84E-05
	5	156609000	rs411174	*ITK*	T	0.31	1.704	0.1282	1.326	2.191	3.17E-05
	15	59981515	rs3087328	*BNIP2*	G	0.42	1.694	0.1276	1.319	2.175	3.66E-05
African-American	1	55304970	rs7549251	*C1orf177*	G	0.39	1.965	0.1519	1.459	2.647	8.74E-06
	3	195489009	rs2246901	*MUC4*	C	0.49	0.529	0.1589	0.3871	0.7217	6.01E-05
	5	112849627	rs116615892	*YTHDC2*	T	0.02	9.551	0.6012	2.94	31.03	0.000174
	1	59799161	rs17119280	*FGGY*	A	0.08	2.609	0.2559	1.58	4.309	0.000179
	11	6790028	rs10839616	*OR2AG2*	G	0.33	1.802	0.163	1.31	2.481	0.000301

*EA= effect allele; **EAF refers to effect allele frequency in the study population

Supplementary Table III. Fixed- and Random-Effects Meta-Analysis Results.

Type	Chr	BP	SNP	Gene	EA	EAF (AFR/EUR)	P Fixed	P Random	OR Fixed	OR Random	Q
All-Stroke	1	55304970	rs7549251	*LEXM (C1orf177)*	G	0.3912/0.3776	4.08E-07	3.32E-06	1.4993	1.5011	0.2751
	4	184612553	rs67383011	*TRAPPC11*	C	0.04864/0.09866	5.19E-06	0.00389	0.5013	0.5225	0.1601
	7	12406989	rs6460939	*VWDE*	G	0.4522/0.4616	8.79E-06	8.79E-06	1.4147	1.4147	0.9893
	8	120052238	rs6993813	*COLEC10*	T	0.2544/0.4762	2.60E-05	2.60E-05	1.4167	1.4167	0.8696
	9	139111870	rs7849585	*QSOX2*	G	0.2384/0.3313	5.32E-05	5.32E-05	0.7109	0.7109	0.8392
Cardioembolic	16	81010073	rs1127390	*CMC2*	T	0.4019/0.2156	5.28E-05	5.28E-05	0.5179	0.5179	0.3212
	11	34637669	rs10836265	*EHF*	A	0.1411/0.3776	6.08E-05	0.001202	1.8553	1.8953	0.2128
	11	120152591	rs11217785	*POU2F3*	T	0.3756/0.2229	0.0001877	0.0001877	1.6794	1.6794	0.9829
	1	161681780	rs2275603	*FCRLA*	G	0.3684/0.2071	0.000258	0.000258	1.7397	1.7397	0.3422
	8	38095662	rs2306899	*DDHD2*	T	0.05263/0.24	0.0002635	0.0002635	1.9208	1.9208	0.3346
Large-Artery	4	88534065	rs3750025	*DSPP*	A	0.01994/0.02558	1.78E-05	1.78E-05	7.3028	7.3028	0.5095
	2	85590286	rs7564372	*ELMOD3*	T	0.1746/0.01644	4.42E-05	0.0946	4.1382	9.063	0.0052
	5	115175503	rs6594908	*ATG12*	G	0.4258/0.00609	4.57E-05	4.57E-05	4.3846	4.3846	0.421
	4	3494898	rs6850908	*DOK7*	T	0.0638/0.2144	6.89E-05	0.1331	2.9793	5.1667	0.0009
	8	27321189	rs56229264	*CHRNA2*	A	0.00319/0.02134	9.55E-05	9.55E-05	8.7194	8.7194	0.3506
Small-Vessel	9	104020751	rs1329071	*LPPR1*	T	0.2663/0.4123	3.85E-05	3.85E-05	1.9029	1.9029	0.5609
	3	147959286	rs1495327	*AGTR1*	G	0.4912/0.257	0.0001439	0.0001439	1.8125	1.8125	0.9273
	4	44682465	rs6447368	*GUF1*	C	0.3485/0.3928	0.0001984	0.0001984	1.7869	1.7869	0.6251
	9	139111870	rs7849585	*QSOX2*	G	0.2384/0.3313	0.0002393	0.0009275	0.5323	0.5331	0.2686
	2	34480075	rs6733379	*LINC01317*	G	0.319/0.2868	0.0002403	0.0002403	1.8151	1.8151	0.5143
Other Known	20	20071521	rs111472581	*CFAP61*	A	0.02233/0.004872	1.81E-06	1.81E-06	20.351	20.351	0.9796
	22	41574383	rs1046088	*EP300*	C	0.004785/0.03776	7.18E-05	7.18E-05	6.397	6.397	0.582
	17	3981290	rs78806449	*ZZEF1*	G	0.0311/0.0609	7.69E-05	7.69E-05	5.6636	5.6636	0.6814
	11	7324584	rs78477754	*SYT9*	A	0.01834/0.02619	0.0001165	0.0001165	6.2698	6.2698	0.6026
	2	47287925	rs140166160	*TTC7A*	A	0.003987/0.007308	0.000117	0.000117	21.2573	21.2573	0.4615
Undetermined	1	55304970	rs7549251	*C1orf177*	G	0.3912/0.3776	1.43E-07	9.85E-05	1.68E+00	1.695	0.1724
	4	184612553	rs67383011	*TRAPPC11*	C	0.04864/0.09866	1.17E-05	4.76E-04	0.3996	0.4104	0.2396
	3	38766675	rs6795970	*SCN10A*	A	0.07735/0.3995	4.54E-05	4.54E-05	1.58E+00	1.5787	0.5585
	3	38774832	rs6800541	*SCN10A*	C	0.07815/0.4026	5.43E-05	5.43E-05	1.57E+00	1.5731	0.5013
	3	151579873	rs6798928	*AADACL2-AS1*	A	0.1914/0.4233	8.57E-05	8.57E-05	6.57E-01	0.6565	0.8866

EA= effect allele; EAF=effect allele frequency in study population (AFR/EUR); OR=Odds Ratio; Q=Cochran's Q.

Supplementary Table IV. Top 10 Pathway analysis results for all-stroke implementing gene-burden test results.

Ingenuity Pathways	P-value	Molecules
Tryptophan Degradation III	6.92E-06	ACAT2, EHHADH, HSD17B8, IDO1, KMO, KYNU
Tryptophan Degradation to 2-amino-3-carboxymuconate Semialdehyde	4.37E-04	IDO1, KMO, KYNU
Fatty Acid Î²-oxidation I	4.37E-04	ACAA1, EHHADH, HSD17B8, SLC27A4, SLC27A5
Cholesterol Biosynthesis I	2.09E-03	DHCR24, FDFT1, LSS
Superpathway of Cholesterol Biosynthesis	2.34E-03	ACAT2, DHCR24, FDFT1, LSS
NAD biosynthesis II (from tryptophan)	3.24E-03	IDO1, KMO, KYNU
Glutaryl-CoA Degradation	3.24E-03	ACAT2, EHHADH, HSD17B8
Type II Diabetes Mellitus Signaling	4.57E-03	FGFR1, MAP3K1, PIK3CG, PIK3R2, SLC27A4, SLC27A5, SMPD1, TNFRSF11B
HMGB1 Signaling	6.03E-03	CNTF, CSF2, FGFR1, IL3, MAP2K3, PIK3CG, PIK3R2, TNFRSF11B
p53 Signaling	7.76E-03	ATR, FGFR1, PIK3CG, PIK3R2, TNFRSF10A, TP53AIP1, TRIM29

Supplementary Table V. ***NAT10*** **SNPs evaluated on Exome-Chip in GEOS (highlighted in yellow) and *NAT10* GWAS lookups in the Young-Onset Stroke Consortium and MEGASTROKE as ordered by SNP location 5´ to 3´, with significantly associated ($p<0.05$) ‘replication’ SNPs (highlighted in green).**

Notably, there were no direct SNP overlaps between the exome chip and GWA studies, as the GWA content includes primarily common variants, while the exome chip includes primarily rare variants.

NA – indicates not available or non-calculable.

Table header description:
RsNum- dbSNP ID,
Position – position in Human Genome Browser - hg19 assembly,
Ref - reference allele,
Alt -alternate allele,
Type - type of variant,
Function,
AA change,
Early_META_no_GEOS - GEOS excluded from ***Cheng et al.* meta-analysis**[3],
MEGA_EUR_SV – **MEGASTROKE**[5] EUROPEAN small vessel summary result,
MEGA_TRANS_SV – **MEGASTROKE**[5] TRANS-ETHNIC small vessel summary result,
SV_META- single variant result from **GEOS** exome chip,
SV_META_population – **GEOS** population specific result reported,
1kg_ALL- minor allele frequency in 1000G all populations,
1kg_AFR - minor allele frequency in AFR samples of 1000 Genomes,
1kg_EUR - minor allele frequency in EUR samples of 1000 Genomes,
ESP_ALL - minor allele frequency in Exome Sequencing Project all samples,
ESP_AA - minor allele frequency in Exome Sequencing Project African-American samples,
ESP_EA - minor allele frequency in Exome Sequencing Project European-American samples.

rsNum	Position	Ref	Alt	Type	Function	AAchg	Early_META_no_GEOS	MEGA_EUR_SV	MEGA_TRANS_SV	SV_META	SV_META_pop	1kG_ALL	1kG_AFR	1kG_EUR	ESP_ALL	ESP_AA	ESP_EA
rs111436298	34125240	C	T	intergenic	NA	NA	0.087917	0.9557	0.4215	NA		0.0835	0.1823	0.0775	NA	NA	NA
rs73501048	34125873	T	A	intergenic	NA	NA	0.098647	0.9499	0.4448	NA		0.0907	0.2042	0.0805	NA	NA	NA
rs80155580	34125887	C	A	intergenic	NA	NA	0.082883	0.914	0.467	NA		0.0607	0.0968	0.0775	NA	NA	NA
rs16925170	34126170	C	T	upstream	NA	NA	0.084463	0.8919	0.462	NA		0.0835	0.1823	0.0775	NA	NA	NA
rs16925173	34126533	G	C	upstream	NA	NA	0.087825	0.8674	0.4872	NA		0.0833	0.1815	0.0775	NA	NA	NA
rs1883958	34127122	C	G	UTR5	NA	NA	0.074237	0.9686	NA	NA		0.0369	0.0083	0.0775	NA	NA	NA
rs16925175	34127463	T	C	intronic	NA	NA	0.045241	0.8447	0.5021	NA		0.0835	0.1823	0.0775	NA	NA	NA
rs79446413	34127472	A	T	intronic	NA	NA	0.041544	0.9991	0.5395	NA		0.0609	0.0976	0.0775	NA	NA	NA
rs79275993	34127657	C	G	intronic	NA	NA	0.625935	NA	NA	NA		0.0028	NA	0.0129	NA	NA	NA
rs79275993	34127657	C	T	intronic	NA	NA	0.625935	NA	NA	NA		NA	NA	NA	NA	NA	NA
rs16925177	34127839	A	G	intronic	NA	NA	0.087796	0.8669	0.4854	NA		0.0835	0.1823	0.0775	NA	NA	NA
rs73501059	34128031	A	G	intronic	NA	NA	0.087027	0.8357	0.4934	NA		0.0649	0.1127	0.0775	NA	NA	NA
rs2024624	34128208	G	C	intronic	NA	NA	0.107332	0.7314	NA	NA		0.0094	0.0023	0.0278	NA	NA	NA
rs117850996	34128782	T	G	intronic	NA	NA	0.347467	0.112	NA	NA		0.0146	NA	0.0249	NA	NA	NA
rs75300173	34128942	A	G	intronic	NA	NA	0.890912	0.04587	NA	NA		0.003	NA	0.0119	NA	NA	NA
rs75129511	34129040	C	T	intronic	NA	NA	0.082692	0.9988	0.5409	NA		0.0609	0.0976	0.0775	NA	NA	NA
rs77103524	34129201	A	G	intronic	NA	NA	0.087723	0.8668	0.4855	NA		0.0833	0.1823	0.0765	NA	NA	NA
rs11032515	34129394	C	T	intronic	NA	NA	0.329881	0.2658	0.1024	NA		0.2097	0.0923	0.2286	NA	NA	NA
rs113967792	34129399	C	A	intronic	NA	NA	0.086995	0.8492	0.485	NA		0.0647	0.1127	0.0765	NA	NA	NA
rs140188192	34129779	C	T	exonic	missense	R3W	NA	NA	NA	NA		4.00E-04	NA	0.002	0.001231	0.0007	0.0015
rs78307936	34130015	C	G	intronic	NA	NA	0.866419	0.0221	NA	NA		0.0727	0.1051	0.1074	NA	NA	NA
rs73501064	34130164	A	G	intronic	NA	NA	0.092457	0.9534	0.4358	NA		0.0843	0.1823	0.0805	NA	NA	NA
rs73501065	34130195	G	A	intronic	NA	NA	0.098385	0.9481	0.4452	NA		0.0907	0.2042	0.0805	NA	NA	NA
rs11552143	34130342	A	G	exonic	synonymou	S54S	0.085249	0.8435	0.4835	NA		0.0649	0.1127	0.0775	0.091846	0.0904	0.0926
rs17700360	34130406	A	G	intronic	NA	NA	0.086903	0.8563	0.4807	NA		0.0649	0.1127	0.0775	0.091846	0.0904	0.0926
rs16925181	34131716	C	T	intronic	NA	NA	0.045048	0.9246	0.451	NA		0.0835	0.1823	0.0775	NA	NA	NA
rs116967665	34131795	G	A	intronic	NA	NA	0.27289	0.8802	NA	NA		0.007	0.0023	0.0209	NA	NA	NA
rs73501069	34131901	A	G	intronic	NA	NA	0.045036	0.8622	0.4894	NA		0.0835	0.1823	0.0775	NA	NA	NA
rs75953991	34132557	G	A	intronic	NA	NA	0.082486	0.9966	0.5374	NA		0.0611	0.0983	0.0775	NA	NA	NA
rs16925182	34132964	C	G	intronic	NA	NA	0.087395	0.8687	0.4837	NA		0.0835	0.1823	0.0775	NA	NA	NA
rs73501073	34133552	T	C	intronic	NA	NA	0.086906	0.8461	0.5003	NA		0.0835	0.1823	0.0775	0.106846	0.1351	0.0924
rs79517378	34133586	T	C	intronic	NA	NA	0.117526	0.7925	0.373	NA		0.0835	0.1823	0.0775	0.047231	0.0681	0.0365
rs78574770	34133587	G	A	intronic	NA	NA	0.110436	0.7949	0.3584	NA		0.0835	0.1823	0.0775	0.052385	0.0745	0.0411
rs17778759	34134698	G	A	intronic	NA	NA	0.081032	0.9997	0.538	NA		0.0607	0.0968	0.0775	NA	NA	NA
rs16925183	34134892	G	A	intronic	NA	NA	0.096111	0.9563	0.4352	NA		0.0847	0.1838	0.0805	NA	NA	NA
rs10836156	34134926	C	T	intronic	NA	NA	0.75177	0.04172	0.007311	NA		0.3652	0.3812	0.4036	NA	NA	NA
rs74497402	34135072	A	G	intronic	NA	NA	0.086778	0.8529	0.4964	NA		0.0835	0.1823	0.0775	NA	NA	NA
rs201730594	34135273	C	G	exonic	missense	A56G	NA	NA	NA	NA		2.00E-04	8.00E-04	NA	NA	NA	NA
rs2957481	34136028	T	C	intronic	NA	NA	0.097591	0.8295	0.5432	NA		0.8942	0.7398	0.9195	NA	NA	NA
rs112380660	34136096	A	G	intronic	NA	NA	0.080786	0.9963	0.5344	NA		0.0607	0.0968	0.0775	NA	NA	NA
rs117309058	34136307	G	A	intronic	NA	NA	0.572844	0.6374	NA	NA		0.0214	0.0015	0.0775	NA	NA	NA
rs181755346	34136544	A	G	intronic	NA	NA	0.045623	NA	NA	NA		0.0024	NA	0.005	NA	NA	NA
rs60494596	34137087	G	A	intronic	NA	NA	0.085671	0.8658	0.4836	NA		0.0835	0.1823	0.0775	NA	NA	NA
rs79996353	34137524	G	A	intronic	NA	NA	0.08077	0.9997	0.5378	NA		0.0607	0.0968	0.0775	NA	NA	NA
rs60015864	34137686	T	C	intronic	NA	NA	0.043601	0.867	0.4822	NA		0.0835	0.1823	0.0775	NA	NA	NA
rs58755000	34137713	T	C	intronic	NA	NA	0.043599	0.8669	0.4822	NA		0.0835	0.1823	0.0775	NA	NA	NA
rs16925184	34137875	G	A	intronic	NA	NA	0.043584	0.8656	0.4836	NA		0.0835	0.1823	0.0775	NA	NA	NA
rs80179115	34137932	T	C	intronic	NA	NA	0.040027	0.9957	0.5408	NA		0.0607	0.0968	0.0775	NA	NA	NA
rs56693007	34138028	C	T	intronic	NA	NA	0.0436	0.8646	0.4849	NA		0.0835	0.1823	0.0775	NA	NA	NA
rs57492451	34138451	A	G	intronic	NA	NA	0.043079	0.8565	0.4763	NA		0.0651	0.1135	0.0775	NA	NA	NA
rs183279686	34138771	T	G	intronic	NA	NA	0.391953	0.0665	NA	NA		0.0126	0.0023	0.0169	NA	NA	NA
rs59158919	34138993	G	A	intronic	NA	NA	0.08495	0.8602	0.4733	NA		0.0649	0.1127	0.0775	NA	NA	NA
rs58696677	34139217	G	A	intronic	NA	NA	0.032991	0.6699	0.6078	NA		0.0937	0.1831	0.1064	NA	NA	NA
rs59518134	34139278	A	C	intronic	NA	NA	0.085744	0.8672	0.4833	NA		0.0835	0.1823	0.0775	NA	NA	NA
rs35674959	34139840	C	T	exonic	missense	P152L	NA	NA	NA	0.5686	(AFR)	0.0052	0.0197	NA	0.005154	0.0152	NA
rs74773419	34140501	A	G	intronic	NA	NA	0.087171	0.9265	NA	NA		0.0341	0.0076	0.0716	NA	NA	NA
rs3751124	34140951	T	C	intronic	NA	NA	0.594461	NA	NA	NA		0.0304	8.00E-04	0.002	NA	NA	NA
rs2957509	34141528	C	T	intronic	NA	NA	0.096692	0.8864	0.791	NA		0.869	0.6467	0.9225	NA	NA	NA
rs75817653	34141632	A	G	intronic	NA	NA	0.089314	0.8936	0.6029	NA		0.0749	0.1437	0.0805	NA	NA	NA
rs73501097	34141875	A	G	intronic	NA	NA	0.094617	0.9869	0.4192	NA		0.0907	0.2042	0.0805	NA	NA	NA
rs11600691	34142340	G	A	intronic	NA	NA	0.801509	0.7379	NA	NA		0.0074	0.0076	0.008	NA	NA	NA
rs190123218	34143497	C	T	intronic	NA	NA	0.922389	0.2331	NA	NA		0.0164	0.0023	0.0477	NA	NA	NA
rs116940567	34144261	G	A	intronic	NA	NA	0.107186	0.7449	NA	NA		0.0096	0.0023	0.0278	NA	NA	NA
rs73500434	34144579	T	C	intronic	NA	NA	0.095499	0.9835	0.3571	NA		0.0958	0.2239	0.0805	NA	NA	NA
rs17700714	34144673	T	C	intronic	NA	NA	0.080721	0.9521	0.5021	NA		0.0607	0.0968	0.0775	NA	NA	NA
rs139800295	34145358	C	G	exonic	missense	L250V	NA	NA	NA	NA		NA	NA	NA	0.000231	0.0007	NA
rs2982587	34146502	A	G	intronic	NA	NA	0.10227	0.9873	0.6429	NA		0.8702	0.6536	0.9195	NA	NA	NA
rs59359577	34147488	A	G	intronic	NA	NA	0.089012	0.9155	0.5993	NA		0.0605	0.0968	0.0775	NA	NA	NA
rs148590717	34147506	C	T	intronic	NA	NA	0.601066	0.6073	NA	NA		0.0218	0.0015	0.0775	NA	NA	NA
rs184953428	34150109	G	A	intronic	NA	NA	NA	0.01469	NA	NA		0.0056	NA	0.0169	NA	NA	NA
rs2957514	34150502	C	T	intronic	NA	NA	0.115879	0.9579	0.5609	NA		0.8295	0.5061	0.9175	NA	NA	NA
rs117072479	34150761	A	T	intronic	NA	NA	0.964802	0.00119	NA	NA		0.0082	NA	0.0229	NA	NA	NA
rs80119048	34150825	T	C	intronic	NA	NA	0.086169	0.9567	0.5713	NA		0.0613	0.0991	0.0775	NA	NA	NA
rs2982619	34150839	C	G	intronic	NA	NA	0.102007	0.9197	0.4502	NA		0.8936	0.7375	0.9195	NA	NA	NA
rs79396490	34150954	A	G	intronic	NA	NA	0.078382	0.9521	NA	NA		0.0369	0.0083	0.0775	NA	NA	NA
rs17700877	34151771	A	G	intronic	NA	NA	0.086353	0.9576	0.5716	NA		0.0613	0.0991	0.0775	NA	NA	NA
rs148211973	34152464	C	T	exonic	missense	T378M	NA	NA	NA	NA		NA	NA	NA	0.000846	NA	0.0013
rs2957516	34152939	T	C	exonic	missense	Y389H	NA	NA	NA	NA		0.9978	0.9917	1	0.997462	0.9925	1
rs146685334	34152973	C	A	exonic	missense	A400D	NA	NA	NA	NA		2.00E-04	NA	0.001	0.000462	NA	0.0007
rs138988892	34153038	C	T	exonic	missense	R422W	NA	NA	NA	NA		NA	NA	NA	0.000154	NA	0.0002
rs12419404	34153107	G	T	intronic	NA	NA	0.537188	0.4405	NA	NA		0.0214	0.0015	0.0775	0.050769	0.0159	0.0686
rs142148595	34153739	A	G	exonic	missense	M458V	NA	NA	NA	NA		NA	NA	NA	0.001077	0.0007	0.0013
rs2982617	34154432	A	G	intronic	NA	NA	0.110337	0.8996	0.8618	NA		0.8838	0.7012	0.9205	NA	NA	NA
rs139767479	34154579	C	T	exonic	missense	P470S	NA	NA	NA	0.1268	(EUR)	0.0018	NA	0.001	0.001	0.0002	0.0014
rs149555377	34154583	A	G	exonic	missense	N471S	NA	NA	NA	0.2938	(AFR)	4.00E-04	8.00E-04	NA	0.000923	0.0027	NA
rs61735311	34154645	C	T	exonic	missense	P492S	0.332247	0.7663	NA	NA		0.0242	8.00E-04	0.0169	0.017154	0.0032	0.0243
rs199661193	34154650	C	G	exonic	synonymou	P493P	NA	NA	NA	NA		0.001	NA	NA	7.70E-05	NA	0.0001
rs200962843	34156107	A	C	exonic	missense	I557L	NA	NA	NA	NA		NA	NA	NA	NA	NA	NA
rs145242316	34156722	A	G	exonic	missense	M566V	NA	NA	NA	NA		0.0072	NA	NA	NA	NA	NA
rs60549862	34157276	T	C	intronic	NA	NA	0.087407	0.9624	0.6005	NA		0.0669	0.118	0.0775	NA	NA	NA
rs149916189	34157709	A	C	intronic	NA	NA	0.573472	0.9743	0.5953	NA		0.0621	0.0998	0.0795	NA	NA	NA
rs145482727	34158274	G	A	exonic	missense	R633H	NA	NA	NA	NA		2.00E-04	NA	0.001	0.001077	NA	0.0016
rs17701015	34160193	C	G	intronic	NA	NA	0.088044	0.9528	0.5999	NA		0.0611	0.0983	0.0775	NA	NA	NA
rs12421526	34160326	T	A	intronic	NA	NA	0.476781	0.2492	0.06354	NA		0.1867	0.0106	0.2306	NA	NA	NA
rs137942423	34160778	C	T	exonic	missense	T679M	NA	NA	NA	NA		4.00E-04	8.00E-04	0.001	0.000462	0.0011	0.0001
rs139525757	34161633	A	G	intronic	NA	NA	0.361875	0.7128	NA	NA		0.0078	0.0023	0.0219	NA	NA	NA
rs2982614	34161907	C	G	intronic	NA	NA	0.215109	0.7923	NA	NA		NA	NA	NA	NA	NA	NA
rs2982614	34161907	C	T	intronic	NA	NA	0.215109	0.7923	NA	NA		0.0224	8.00E-04	0.0119	0.012231	0.0068	0.015
rs79872650	34162549	G	A	intronic	NA	NA	0.746287	0.7308	NA	NA		0.0032	NA	0.0099	NA	NA	NA
rs151223396	34162706	C	T	exonic	missense	S816L	NA	NA	NA	NA		6.00E-04	NA	NA	NA	NA	NA
rs11032530	34162887	C	G	intronic	NA	NA	0.414635	0.9992	0.2634	NA		0.1573	0.0696	0.1252	NA	NA	NA
rs140934116	34163339	C	T	exonic	missense	T857M	NA	NA	NA	0.4436	(AFR)	0.001	0.0038	NA	0.001	0.003	NA
rs145087510	34163688	A	G	intronic	NA	NA	0.140248	0.3889	NA	NA		0.0124	0.0023	0.0189	NA	NA	NA
rs16925219	34164083	C	T	intronic	NA	NA	0.088413	0.9702	0.6144	NA		0.0673	0.1195	0.0775	NA	NA	NA
rs142960948	34165044	G	A	exonic	missense	G908R	NA	NA	NA	0.2131	(EUR)	0.0014	NA	0.006	0.002231	0.0002	0.0033
rs36006049	34165053	G	A	exonic	missense	A911T	NA	NA	NA	0.000693	(AFR)	0.0052	0.0151	0.003	0.006308	0.0089	0.005
rs143930117	34165057	C	T	exonic	missense	S912L	NA	NA	NA	NA		NA	NA	NA	0.000154	NA	0.0002
rs72910804	34165079	A	G	intronic	NA	NA	0.935501	0.4391	NA	NA		0.009	0.0038	0.0249	0.019615	0.0066	0.0263
rs7933297	34167180	T	C	intronic	NA	NA	0.089308	0.9704	NA	NA		0.0619	0.1021	0.0775	NA	NA	NA
rs116888571	34167531	C	T	intronic	NA	NA	0.836642	0.3633	NA	NA		0.0062	NA	0.0169	NA	NA	NA
rs200149938	34167709	A	T	exonic	missense	K944N	NA	NA	NA	NA		2.00E-04	NA	NA	NA	NA	NA
rs139546360	34167728	C	T	exonic	missense	R951W	NA	NA	NA	NA		2.00E-04	NA	0.001	0.000308	NA	0.0005
rs1983642	34167825	C	G	UTR3	NA	NA	0.7799	0.3634	NA	NA		0.0024	NA	0.0109	NA	NA	NA
rs8187	34168153	G	A	UTR3	NA	NA	0.601078	0.2889	0.6104	NA		0.2482	0.0961	0.1481	NA	NA	NA
rs2467392	34169879	A	C	intergenic	NA	NA	0.111104	0.9514	0.3952	NA		0.0968	0.2292	0.0805	NA	NA	NA
rs10501133	34169960	C	T	intergenic	NA	NA	0.088845	0.9844	0.47	NA		0.0577	0.087	0.0775	NA	NA	NA
rs2467393	34170562	T	G	intergenic	NA	NA	0.11771	0.9229	0.6524	NA		0.8732	0.6619	0.9195	NA	NA	NA
rs2473932	34170701	T	C	intergenic	NA	NA	0.099374	0.8447	0.4643	NA		0.0968	0.2292	0.0805	NA	NA	NA
rs76458769	34171098	T	G	intergenic	NA	NA	0.27546	0.6292	NA	NA		0.0156	8.00E-04	0.0507	NA	NA	NA
rs80327384	34171389	C	T	intergenic	NA	NA	0.957977	0.007295	NA	NA		0.0411	0.0068	0.0934	NA	NA	NA

Supplementary Figure I. **Meta-Analysis Association Results for All-Stroke: Manhattan and Q-Q Plot.**