Shi *et al.* Genome Sequencing Reveals the Role of Rare Genomic Variants in Chinese Patients with Symptomatic Intracranial Atherosclerotic Disease

SUPPLEMENTAL MATERIALS

eTable 1. Genes related to stroke or other stroke subtypes in monogenic traits

No.	Cytogenetic location	Inheritance	OMIM(#)	*Gene*	Category	Reference (PMID)
1	17q25	AD/AR	{Moyamoya disease 2, susceptibility to}, 607151 (3)	*RNF213*	2	32440785; 23010677
2	19p13.2	AD	Hypercholesterolemia, familial, 1, 143890 (3); LDL cholesterol level QTL2, 143890 (3)	*LDLR*	1.2	27809445
3	2p24	AR/AD	Hypobetalipoproteinemia, 615558 (3); Hypercholesterolemia, familial, 2, 144010 (3)	*APOB*	1.2	27809445
4	1p32.3	AD	Hypercholesterolemia, familial, 3, 603776 (3),; {Low density lipoprotein cholesterol level QTL 1}, 603776 (3)	*PCSK9*	1.2	27809445
5	1p36-p35	AR	Hypercholesterolemia, familial, 4, 603813 (3)	*LDLRAP1*	1.2	27809445
6	2p21	AR	Sitosterolemia 2, 618666 (3)	*ABCG5*	1.2	27809445
7	2p21	AR	{Gallbladder disease 4}, 611465 (3); Sitosterolemia 1, 210250 (3)	*ABCG8*	1.2	27809445
8	10q23.31	AR	Wolman disease, 278000 (3); Cholesteryl ester storage disease, 278000 (3)	*LIPA*	1.2	27809445
9	2q33-qter	AR	Cerebrotendinous xanthomatosis, 213700 (3)	*CYP27A1*	1.2	27809445
10	NA	AD	{Coronary artery disease, autosomal dominant, 2};Tooth agenesis, selective, 7,616724(3)	*LRP6*	1.2	27809445
11	19q13.2	AR	Hyperlipoproteinemia, type Ib, 207750 (3)	*APOC2*	1.2	27809445
12	16p13.3	AR	Lipase deficiency, combined, 246650 (3)	*LMF1*	1.2	27809445
13	11q23	AD	{Hypertriglyceridemia, susceptibility to}, 145750 (3); Hyperchylomicronemia, late-onset, 144650 (3)	*APOA5*	1.2	27809445
14	8q24.3	AR	Hyperlipoproteinemia, type 1D, 615947 (3)	*GPIHBP1*	1.2	27809445
15	1q22-q23	NA	{Hyperlipidemia, familial combined, susceptibility to}, 602491 (3)	*USF1*	1.2	27809445
16	15q21.3	AR/AD	[High density lipoprotein cholesterol level QTL 12], 612797 (3); Hepatic lipase deficiency, 614025 (3); {Diabetes mellitus, noninsulin-dependent}, 125853 (3)	*HL*	1.2	27809445
17	3p25	AR/AD	[Obesity, resistance to] (3); Carotid intimal medial thickness 1, 609338 (3); {Diabetes, type 2}, 125853 (3); Insulin resistance, severe, digenic, 604367 (3); Obesity, severe, 601665 (3); Lipodystrophy, familial partial, type 3, 604367 (3)	*PPARG*	1.2	27809445
18	1p36.22	NA	NA	*TNFRSF1B*	1.2	27809445
19	8p22	AR/AD	Lipoprotein lipase deficiency, 238600 (3); [High density lipoprotein cholesterol level QTL 11], 238600 (3); Combined hyperlipidemia, familial, 144250 (3)	*LPL*	1.2	27809445
20	15q21.3	AR/AD	[High density lipoprotein cholesterol level QTL 12], 612797 (3); Hepatic lipase deficiency, 614025 (3); {Diabetes mellitus, noninsulin-dependent}, 125853 (3)	*LIPC*	1.2	27809445
21	11q23	AD	Hypoalphalipoproteinemia, primary, 2, with or without corneal clouding, 618463 (3); Amyloidosis, 3 or more types, 105200 (3), Autosomal dominant; ApoA-I and apoC-III deficiency, combined, 618463 (3)	*APOA1*	1.2	27809445

22	19q13.2	AR/AD	Hyperlipoproteinemia, type III, 617347 (3); {Coronary artery disease, severe, susceptibility to}, 617347 (3); {?Alzheimer disease, protection against, due to APOE3-Christchurch}, 607822 (3); Lipoprotein glomerulopathy, 611771 (3); Sea-blue histiocyte disease, 269600 (3); {?Macular degeneration, age-related}, 603075 (3), Autosomal dominant; Alzheimer disease 2, 104310 (3)	*APOE*	1.2	27809445
23	2p23.3	NA	[Fasting plasma glucose level QTL 5],613463	*GCKR*	1.2	24879641
24	12p13	AR/AD	Pseudohypoaldosteronism, type IIC, 614492 (3); Neuropathy, hereditary sensory and autonomic, type II, 201300 (3)	*WNK1*	1.1	31577254
25	17q21-q22	AD	Pseudohypoaldosteronism, type IIB, 614491 (3)	*WNK4*	1.1	31577254
26	12p12.2	AD	Hypertension and brachydactyly syndrome, 112410 (3)	*PDE3A*	1.1	31577254
27	8q21	AR/AD	Adrenal hyperplasia, congenital, due to 11-beta-hydroxylase deficiency, 202010 (3); Aldosteronism, glucocorticoid-remediable, 103900 (3)	*CYP11B1*	1.1	31577254
28	5q31	AR/AD	Pseudohypoaldosteronism, type IID, 614495 (3)	*KLHL3*	1.1	31577254
29	2q36	AD	Pseudohypoaldosteronism, type IIE, 614496 (3)	*CUL3*	1.1	31577254
30	4q31.1	AD	Pseudohypoaldosteronism type I, autosomal dominant, 177735 (3); Hypertension, early-onset, autosomal dominant, with exacerbation in pregnancy, 605115 (3)	*NR3C2*	1.1	31577254
31	16p13-p12	AR/AD	Bronchiectasis with or without elevated sweat chloride 1, 211400 (3); Pseudohypoaldosteronism, type I, 264350 (3), Autosomal recessive; Liddle syndrome 1, 177200 (3), Autosomal dominant	*SCNN1B*	1.1	31577254
32	16p13-p12	AR/AD	Bronchiectasis with or without elevated sweat chloride 3, 613071 (3); Liddle syndrome 2, 618114 (3), Autosomal dominant; Pseudohypoaldosteronism, type I, 264350 (3)	*SCNN1G*	1.1	31577254
33	16q22	AR	Apparent mineralocorticoid excess, 218030 (3)	*HSD11B2*	1.1	31577254
34	10q24.3	AR	17-alpha-hydroxylase/17,20-lyase deficiency, 202110 (3); 17,20-lyase deficiency, isolated, 202110 (3)	*CYP17A1*	1.1	31577254
35	12p13	AR/AD	Pseudohypoaldosteronism, type I, 264350 (3); ?Liddle syndrome 3, 618126 (3); Bronchiectasis with or without elevated sweat chloride 2, 613021 (3)	*SCNN1A*	1.1	31577254
36	12q24.2	AR/AD	{Diabetes mellitus, insulin-dependent}, 222100 (3); MODY, type III, 600496 (3); Hepatic adenoma, somatic, 142330 (3); Renal cell carcinoma, 144700 (3); Diabetes mellitus, insulin-dependent, 20, 612520 (3); {Diabetes mellitus, noninsulin-dependent, 2}, 125853 (3)	*HNF1A*	1.3	30377832
37	20q12-q13.1	AD	{Diabetes mellitus, noninsulin-dependent}, 125853 (3); MODY, type I, 125850 (3),	*HNF4A*	1.3	30377832

			Autosomal dominant; Fanconi renotubular syndrome 4, with maturity-onset diabetes of the young, 616026 (3)			
38	17q12	AD	Diabetes mellitus, noninsulin-dependent, 125853 (3); Renal cysts and diabetes syndrome, 137920 (3); {Renal cell carcinoma}, 144700 (3)	*HNF1B*	1.3	30377832
39	11p15.1	AR/AD	Diabetes mellitus, permanent neonatal, 606176 (3); Diabetes mellitus, noninsulin-dependent, 125853 (3); Diabetes mellitus, transient neonatal 2, 610374 (3); Hyperinsulinemic hypoglycemia, familial, 1, 256450 (3); Hypoglycemia of infancy, leucine-sensitive, 240800 (3)	*ABCC8*	1.3	30377832
40	11p15.1	AR/AD	Maturity-onset diabetes of the young, type 13, 616329 (3); {Diabetes mellitus, type 2, susceptibility to}, 125853 (3); Diabetes, permanent neonatal, with or without neurologic features, 606176 (3); Diabetes mellitus, transient neonatal, 3, 610582 (3); Hyperinsulinemic hypoglycemia, familial, 2, 601820 (3)	*KCNJ11*	1.3	30377832
41	11p15.5	AR/AD	Maturity-onset diabetes of the young, type 10, 613370 (3); Hyperproinsulinemia, 616214 (3); Diabetes mellitus, insulin-dependent, 2, 125852 (3); Diabetes mellitus, permanent neonatal, 606176 (3)	*INS*	1.3	30377832
42	2q32	AD	Maturity-onset diabetes of the young 6, 606394 (3); {Diabetes mellitus, noninsulin-dependent}, 125853 (3)	*NEUROD1*	1.3	30377832
43	13q12.1	AR/AD	{Diabetes mellitus, type II, susceptibility to}, 125853 (3); Pancreatic agenesis 1, 260370 (3); MODY, type IV, 606392 (3)	*IPF1*	1.3	30377832
44	9q34.3	AD	Maturity-onset diabetes of the young, type VIII, 609812 (3)	*CEL*	1.3	30377832
45	NA	AD	Wolfram-like syndrome, autosomal dominant, 614296 (3)	*WSF1*	1.3	30377832
46	6q22.2	AR	Mitchell-Riley syndrome, 615710 (3)	*RFX6*	1.3	30377832
47	3p21.1-p14.3	AD	{Maturity-onset diabetes of the young, type 14}, 616511 (3)	*APPL1*	1.3	30377832
48	18q11.1-q11.2	AD	Pancreatic agenesis and congenital heart defects, 600001 (3); Atrial septal defect 9, 614475 (3); Atrioventricular septal defect 5, 614474 (3); Persistent truncus arteriosus, 217095 (3); Tetralogy of Fallot, 187500 (3)	*GATA6*	1.3	30377832
49	10p12.3	AR	Pancreatic and cerebellar agenesis, 609069 (3); Pancreatic agenesis 2, 615935 (3)	*PTF1A*	1.3	30377832
50	2p12	AR	Wolcott-Rallison syndrome, 226980 (3)	*EIF2AK3*	1.3	30377832
51	7p15-p13	AR/AD	Diabetes mellitus, noninsulin-dependent, late onset, 125853 (3); Diabetes mellitus, permanent neonatal, 606176 (3); MODY, type II, 125851 (3), Autosomal dominant; Hyperinsulinemic hypoglycemia, familial, 3, 602485 (3)	*GCK*	1.3	30377832
52	1p34.1	AR	Methylmalonic aciduria and homocystinuria, cblC type, 277400 (3)	*MMACHC*	2	30356112*
53	1p36.22	AR	{Vascular disease, susceptibility to} (3); {Schizophrenia, susceptibility to}, 181500 (3); Homocystinuria due to MTHFR	*MTHFR*	2	30356112*

			deficiency, 236250 (3); {Neural tube defects, susceptibility to}, 601634 (3); {Thromboembolism, susceptibility to}, 188050 (3)			
54	1p36.22	AR	Ehlers-Danlos syndrome, kyphoscoliotic type, 1, 225400 (3)	*PLOD1*	2	30356112*
55	1p36.22	AD	Hereditary motor and sensory neuropathy VIA, 601152 (3); Charcot-Marie-Tooth disease, axonal, type 2A2B, 617087 (3), Autosomal recessive; Charcot-Marie-Tooth disease, axonal, type 2A2A, 609260 (3)	*MFN2*	2	30356112*
56	1q22	AR	Grange syndrome, 602531 (3)	*YY1AP1*	2	30356112*
57	1q22	AD/AR	Muscular dystrophy, congenital, 613205 (3); Lipodystrophy, familial partial, type 2, 151660 (3), Autosomal dominant; Charcot-Marie-Tooth disease, type 2B1, 605588 (3) Cardiomyopathy, dilated, 1A, 115200 (3) ; Heart-hand syndrome, Slovenian type, 610140 (3),; Hutchinson-Gilford progeria, 176670 (3); Restrictive dermopathy, lethal, 275210 (3); Mandibuloacral dysplasia, 248370 (3); Emery-Dreifuss muscular dystrophy 2, 181350 (3); Emery-Dreifuss muscular dystrophy 3, 616516 (3); Malouf syndrome, 212112 (3)	*LMNA*	2	30356112*
58	1q23.3	AD	Thrombocytopenic purpura, autoimmune, 188030 (1),	*FCGR2C*	2	30356112*
59	1q24.2	AD,/ AR	{Pregnancy loss, recurrent, susceptibility to, 1}, 614389 (3); Thrombophilia due to activated protein C resistance, 188055 (3); {Thrombophilia, susceptibility to, due to factor V Leiden}, 188055 (3), ; Factor V deficiency, 227400 (3); {Budd-Chiari syndrome}, 600880 (3); {Stroke, ischemic, susceptibility to}, 601367 (3), Multifactorial	*F5*	2	30356112*
60	1q24.2	AR	Thiamine-responsive megaloblastic anemia syndrome, 249270 (3)	*SLC19A2*	2	30356112*
61	1q32	AD	Glomerulopathy with fibronectin deposits 1, 137950 (2)	*GFND1*	2	30356112*
62	1q41	AD	Loeys-Dietz syndrome 4, 614816 (3)	*TGFB2*	2	30356112*
63	1q42.13	AR	Coenzyme Q10 deficiency, primary, 4, 612016 (3)	*ADCK3*	2	30356112*
64	2p11.2	AD/AR	Vitamin K-dependent clotting factors, combined deficiency of, 1, 277450 (3); Pseudoxanthoma elasticum-like disorder with multiple coagulation factor deficiency, 610842 (3)	*GGCX*	2	30356112*
65	2q14.3	AD/AR	Thrombophilia due to protein C deficiency, autosomal dominant, 176860(3); Thrombophilia due to protein C deficiency, autosomal recessive, 612304 (3)	*PROC*	2	30356112*
66	2q32.2	AD	Immunodeficiency 31C, autosomal dominant, 614162 (3); Immunodeficiency 31A, mycobacteriosis, autosomal dominant, 614892 (3); Immunodeficiency 31B, mycobacterial and viral infections, autosomal recessive, 613796 (3)	*STAT1*	2	30356112*

67	2q32.2	AD	Ehlers-Danlos syndrome, vascular type, 130050 (3); Polymicrogyria with or without vascular-type EDS, 618343 (3)	*COL3A1*	2	30356112*
68	2q32.2	AD	Ehlers-Danlos syndrome, classic type, 2, 130010 (3)	*COL5A2*	2	30356112*
69	2q34	AR/ND	Carbamoylphosphate synthetase I deficiency, 237300 (3); {Pulmonary hypertension, neonatal, susceptibility to}, 615371 (3)	*CPS1*	2	30356112*
70	2q35	AR	Schimke immunoosseous dysplasia, 242900 (3)	*SMARCAL1*	2	30356112*
71	3p21.31	AD	{Systemic lupus erythematosus, susceptibility to}, 152700 (3); Vasculopathy, retinal, with cerebral leukodystrophy, 192315 (3); Aicardi-Goutieres syndrome 1, dominant and recessive, 225750 (3); Chilblain lupus, 610448 (3)	*TREX1*	2	30356112*
72	3p24.1	AD	Esophageal cancer, somatic, 133239 (3); Colorectal cancer, hereditary nonpolyposis, type 6, 614331 (3); Loeys-Dietz syndrome 2, 610168 (3)	*TGFBR2*	2	30356112*
73	3p25.3	AR	Pheochromocytoma, 171300 (3) ; Erythrocytosis, familial, 2, 263400 (3); von Hippel-Lindau syndrome, 193300 (3); Renal cell carcinoma, somatic, 144700 (3); Hemangioblastoma, cerebellar, somatic (3)	*VHL*	2	30356112*
74	3q11.1	AR	Thrombophilia due to protein S deficiency, autosomal recessive, 614514 (3); Thrombophilia due to protein S deficiency, Autosomal dominant, 612336 (3)	*PROS1*	2	30356112*
75	3q21.3	AR	Mitochondrial complex I deficiency, nuclear type 20, 611126 (3)	*ACAD9*	2	30356112*
76	3q22.3	AR	Propionicacidemia, 606054 (3)	*PCCB*	2	30356112*
77	3q26.1	AD	Cerebral cavernous malformations 3, 603285 (3)	*PDCD10*	2	30356112*
78	3q27.3	AR	[Kininogen deficiency], 228960 (3) ; [High molecular weight kininogen deficiency], 228960 (3)	*KNG1*	2	30356112*
79	4q31.3	AR	Dysfibrinogenemia, congenital, 616004 (3); Amyloidosis, familial visceral, 105200 (3); Hypodysfibrinogenemia, congenital, 616004 (3); Afibrinogenemia, congenital, 202400 (3)	*FGA*	2	30356112*
80	4q31.3	AR	Dysfibrinogenemia, congenital, 616004 (3); Afibrinogenemia, congenital, 202400 (3) ; Hypofibrinogenemia, congenital, 202400 (3)	*FGB*	2	30356112*
81	4q32.1	AR	Hypofibrinogenemia, congenital, 202400 (3); Hypodysfibrinogenemia, 616004 (3); Dysfibrinogenemia, congenital, 616004 (3); Afibrinogenemia, congenital, 202400 (3)	*FGG*	2	30356112*
82	4q32.1	AR	Moyamoya 6 with achalasia, 615750 (3)	*GUCY1A3*	2	30356112*
83	5q14.3	AD/somatic	Capillary malformation-arteriovenous malformation 1, 608354 (3); Basal cell carcinoma, somatic, 605462 (3)	*RASA1*	2	30356112*
84	5q33.1	AR	Osteogenesis imperfecta, type XVII, 616507 (3)	*SPARC*	2	30356112*

85	6p12.3	AD/AR	Methylmalonic aciduria, mut(0) type, 251000 (3)	*MUT*	2	30356112*
86	6p25.1	AR	{Myocardial infarction, protection against}, 608446 (3); Factor XIIIA deficiency, 613225 (3); {Venous thrombosis, protection against}, 188050 (3)	*F13A1*	2	30356112*
87	6p25.3	AD/ND	Axenfeld-Rieger syndrome, type 3, 602482 (3); Anterior segment dysgenesis 3, multiple subtypes, 601631 (3)	*FOXC1*	2	30356112*
88	6q23.2	AR	Hypophosphatemic rickets, autosomal recessive, 2, 613312 (3); Cole disease, 615522 (3); {Obesity, susceptibility to}, 601665 (3); Arterial calcification, generalized, of infancy, 1, 208000 (3); {Diabetes mellitus, non-insulin-dependent, susceptibility to}, 125853 (3)	*ENPP1*	2	30356112*
89	6q26	AR	Dysplasminogenemia, 217090 (3); Plasminogen deficiency, type I, 217090 (3)	*PLG*	2	30356112*
90	7p13	AD	Cerebral cavernous malformations-2, 603284 (3)	*C7orf22*	2	30356112*
91	7p14	AD	Telangiectasia, hereditary hemorrhagic, type 4, 610655 (2)	*HHT4*	2	30356112*
92	7q21.2	AD	Cavernous malformations of CNS and retina, 116860 (3); Cerebral cavernous malformations-1, 116860 (3); Hyperkeratotic cutaneous capillary-venous malformations associated with cerebral capillary malformations, 116860 (3)	*CCM1*	2	30356112*
93	7q22.1	AD/AR	{Transcription of plasminogen activator inhibitor, modulator of} (3); Plasminogen activator inhibitor-1 deficiency, 613329 (3)	*SERPINE1*	2	30356112*
94	7q22.1	AR	Lysyl hydroxylase 3 deficiency, 612394 (3)	*PLOD3*	2	30356112*
95	8p21.1	AR	Roberts syndrome, 268300 (3); SC phocomelia syndrome, 269000 (3)	*ESCO2*	2	30356112*
96	9p24.1	AD/somatic	Myelofibrosis, somatic, 254450 (3); Thrombocythemia 3, 614521 (3); Polycythemia vera, somatic, 263300 (3); {Budd-Chiari syndrome, somatic}, 600880 (3); Leukemia, acute myeloid, somatic, 601626 (3); Erythrocytosis, somatic, 133100 (3)	*JAK2*	2	30356112*
97	9q22.33	AD	Loeys-Dietz syndrome 1, 609192 (3) ; {Multiple self-healing squamous epithelioma, susceptibility to}, 132800 (3)	*TGFBR1*	2	30356112*
98	9q31.1	AR	HDL deficiency, familial, 1, 604091 (3); Tangier disease, 205400 (3)	*ABCA1*	2	30356112*
99	9q34.11	AD	Telangiectasia, hereditary hemorrhagic, type 1, 187300 (3)	*ENG*	2	30356112*
100	9q34.11	AR	Citrullinemia, 215700 (3)	*ASS1*	2	30356112*
101	9q34.13	AD	Tuberous sclerosis-1, 191100 (3); Focal cortical dysplasia, type II, somatic, 607341 (3); Lymphangioleiomyomatosis, 606690 (3)	*TSC1*	2	30356112*
102	9q34.3	AD	Ehlers-Danlos syndrome, classic type, 1, 130000 (3)	*COL5A1*	2	30356112*
103	10p14	AD	Hypoparathyroidism, sensorineural deafness, and renal dysplasia, 146255 (3)	*GATA3*	2	30356112*

104	10q23.31	AD	Aortic aneurysm, familial thoracic 6, 611788 (3); Multisystemic smooth muscle dysfunction syndrome, 613834 (3); Moyamoya disease 5, 614042 (3)	*ACTA2*	2	30356112*
105	10q26.13	AD/AR	{Macular degeneration, age-related, neovascular type}, 610149 (3); {Macular degeneration, age-related, 7}, 610149 (3); Cerebral arteriopathy, autosomal dominant, with subcortical infarcts and leukoencephalopathy, type 2, 616779 (3); CARASIL syndrome, 600142 (3)	*HTRA1*	2	30356112*
106	11p11.2	AD	{Pregnancy loss, recurrent, susceptibility to, 2}, 614390 (3); Hypoprothrombinemia, 613679 (3); Dysprothrombinemia, 613679 (3), Autosomal recessive; Thrombophilia due to thrombin defect, 188050 (3); {Stroke, ischemic, susceptibility to}, 601367 (3), Multifactorial	*F2*	2	30356112*
107	11p13	AR	Hemolytic anemia, CD59-mediated, with or without immune-mediated polyneuropathy, 612300 (3)	*CD59*	2	30356112*
108	11p15.4	AD/AR	Myopathy, tubular aggregate, 1, 160565 (3); Immunodeficiency 10, 612783 (3) ; Stormorken syndrome, 185070 (3),	*STIM1*	2	30356112*
109	11p15.4	AR	Thalassemia, beta, 613985 (3); Methmoglobinemia, beta type, 617971 (3); Erythrocytosis 6, 617980 (3); Heinz body anemia, 140700 (3); Delta-beta thalassemia, 141749 (3) ; Thalassemia-beta, dominant inclusion-body, 603902 (3); Hereditary persistence of fetal hemoglobin, 141749 (3); {Malaria, resistance to}, 611162 (3); Sickle cell anemia, 603903 (3)	*HBB*	2	30356112*
110	11q25	AR	Hemorrhagic destruction of the brain, subependymal calcification, and cataracts, 613730 (3)	*JAM3*	2	30356112*
111	11q13.1	AR	Cutis laxa, autosomal recessive, type IB, 614437 (3)	*EFEMP2*	2	30356112*
112	12p13.31	AD	Ehlers-Danlos syndrome, periodontal type, 1, 130080 (3)	*C1R*	2	30356112*
113	12p13.31	AD	Aortic aneurysm, familial thoracic 9, 616166 (3)	*MFAP5*	2	30356112*
114	12q13.13	AD	Telangiectasia, hereditary hemorrhagic, type 2, 600376 (3)	*ACVRL1*	2	30356112*
115	12q24.13	AD	LEOPARD syndrome 1, 151100 (3); Metachondromatosis, 156250 (3) ; Noonan syndrome 1, 163950 (3) ; Leukemia, juvenile myelomonocytic, somatic, 607785 (3)	*PTPN11*	2	30356112*
116	13q14.11	AR	Congenital disorder of glycosylation, type IIl, 614576 (3) ; Shaheen syndrome, 615328 (3)	*COG6*	2	30356112*
117	13q14.2	AD	Dementia, familial British, 176500 (3) ; ?Retinal dystrophy with inner retinal dysfunction and ganglion cell abnormalities, 616079 (3) ; Dementia, familial Danish, 117300 (3)	*ITM2B*	2	30356112*
118	13q34	AD	Angiopathy, hereditary, with nephropathy, aneurysms, and muscle cramps, 611773 (3); Brain small vessel disease with or	*COL4A1*	2	30356112*

			without ocular anomalies, 175780 (3); {Hemorrhage, intracerebral, susceptibility to}, 614519 (3); ?Retinal arteries, tortuosity of, 180000 (3); Microangiopathy and leukoencephalopathy, pontine, autosomal dominant, 618564 (3)			
119	13q32.3	AR	Propionicacidemia, 606054 (3)	*PCCA*	2	30356112*
120	13q34	AD	Brain small vessel disease 2, 614483 (3); {Hemorrhage, intracerebral, susceptibility to}, 614519 (3)	*COL4A2*	2	30356112*
121	13q34	AR	{Myocardial infarction, decreased susceptibility to}, 608446 (3); Factor VII deficiency, 227500 (3)	*F7*	2	30356112*
122	13q34	AR	Factor X deficiency, 227600 (3)	*F10*	2	30356112*
123	14q24.3	AD	Loeys-Dietz syndrome 5, 615582 (3),; Arrhythmogenic right ventricular dysplasia 1, 107970 (3)	*TGFB3*	2	30356112*
124	15q21.1	AD	Marfan lipodystrophy syndrome, 616914 (3) ; Marfan syndrome, 154700 (3) ; MASS syndrome, 604308 (3); Ectopia lentis, familial, 129600 (3) ; Acromicric dysplasia, 102370 (3); Weill-Marchesani syndrome 2, dominant, 608328 (3); Geleophysic dysplasia 2, 614185 (3); Stiff skin syndrome, 184900 (3)	*FBN1*	2	30356112*
125	15q15.1	AR	Isovaleric acidemia, 243500 (3)	*IVD*	2	30356112*
126	16p13.11	AD	Aortic aneurysm, familial thoracic 4, 132900 (3)	*MYH11*	2	30356112*
127	15q22.33	AD	Loeys-Dietz syndrome 3, 613795 (3)	*SMAD3*	2	30356112*
128	16p13.11	AD/AR	Arterial calcification, generalized of infancy, 2, 614473(3); Pseudoxanthoma elasticum, 264800,(3); Pseudoxanthoma elasticum, forme fruste,177850 (3)	*ABCC6*	2	30356112*
129	16p13.3	AD	Tuberous sclerosis-2, 613254 (3) ; ?Focal cortical dysplasia, type II, somatic, 607341 (3); Lymphangioleiomyomatosis, somatic, 606690 (3)	*TSC2*	2	30356112*
130	16p13.3	AD	Polycystic kidney disease 1, 173900 (3)	*PKD1*	2	30356112*
131	17q11.2	AD	Neurofibromatosis-Noonan syndrome, 601321 (3); Leukemia, juvenile myelomonocytic, 607785 (3); Neurofibromatosis, familial spinal, 162210 (3); Watson syndrome, 193520 (3); Neurofibromatosis, type 1, 162200 (3)	*NF1*	2	30356112*
132	17q21.33	AD	Osteogenesis imperfecta, type I, 166200 (3); Osteogenesis imperfecta, type IV, 166220 (3) ; Osteogenesis imperfecta, type II, 166210 (3); {Bone mineral density variation QTL, osteoporosis}, 166710 (3) ; Caffey disease, 114000 (3); Ehlers-Danlos syndrome, arthrochalasia type, 1, 130060 (3); Osteogenesis imperfecta, type III, 259420 (3)	*COL1A1*	2	30356112*
133	17q25.3	AR	Glycogen storage disease II, 232300 (3)	*GAA*	2	30356112*
134	18q12.1	AD	Amyloidosis, hereditary, transthyretin-related, 105210 (3); [Dystransthyretinemic hyperthyroxinemia], 145680 (3), Autosomal dominant; Carpal tunnel syndrome, familial, 115430 (3)	*TTR*	2	30356112*

135	18q21.2	AD	Polyposis, juvenile intestinal, 174900 (3); Juvenile polyposis/hereditary hemorrhagic telangiectasia syndrome, 175050 (3); Myhre syndrome, 139210 (3) ; Pancreatic cancer, somatic, 260350 (3)	*SMAD4*	2	30356112*
136	19p13.12	AD	?Myofibromatosis, infantile 2, 615293 (3); Cerebral arteriopathy with subcortical infarcts and leukoencephalopathy 1, 125310 (3); Lateral meningocele syndrome, 130720 (3)	*NOTCH3*	2	30356112*
137	19p13.13	AR	Glutaricaciduria, type I, 231670 (3)	*GCDH*	2	30356112*
138	19p13.2	AR	Spondyloenchondrodysplasia with immune dysregulation, 607944 (3)	*ACP5*	2	30356112*
139	19p13.13	AD	Spinocerebellar ataxia 6, 183086 (3); Epileptic encephalopathy, early infantile, 42, 617106 (3); Migraine, familial hemiplegic, 1, with progressive cerebellar ataxia, 141500 (3); Episodic ataxia, type 2, 108500 (3); Migraine, familial hemiplegic, 1, 141500 (3)	*CACNA1A*	2	30356112*
140	19q13.2	AD	Abdominal obesity-metabolic syndrome 3, 615812 (3)	*DYRK1B*	2	30356112*
141	20p11.21	AD	Thrombophilia due to thrombomodulin defect, 614486 (3); {Hemolytic uremic syndrome, atypical, susceptibility to, 6}, 612926 (3)	*THBD*	2	30356112*
142	20p11.21	AD	Cerebral amyloid angiopathy, 105150 (3); {Macular degeneration, age-related, 11}, 611953 (3)	*CST3*	2	30356112*
143	20p12.2	AD	?Deafness, congenital heart defects, and posterior embryotoxon, 617992 (3); Alagille syndrome 1, 118450 (3); Tetralogy of Fallot, 187500 (3)	*JAG1*	2	30356112*
144	20q11.23	AR/AD	?Chilblain lupus 2, 614415 (3) ; Aicardi-Goutieres syndrome 5, 612952 (3)	*SAMHD1*	2	30356112*
145	20q13.12	AR	Galactosialidosis, 256540 (3)	*CTSA*	2	30356112*
146	20q13.12	AR	Arterial tortuosity syndrome, 208050 (3)	*SLC2A10*	2	30356112*
147	21q21.3	AD	Cerebral amyloid angiopathy, Dutch, Italian, Iowa, Flemish, Arctic variants, 605714 (3); Alzheimer disease 1, familial, 104300 (3)	*APP*	2	30356112*
148	21q22.3	AR	Homocystinuria, B6-responsive and nonresponsive types, 236200 (3); Thrombosis, hyperhomocysteinemic, 236200 (3)	*CBS*	2	30356112*
149	21q22.3	AR	Microcephalic osteodysplastic primordial dwarfism, type II, 210720 (3)	*PCNT*	2	30356112*
150	22q11.1	AR	Vasculitis, autoinflammation, immunodeficiency, and hematologic defects syndrome, 615688 (3); ?Sneddon syndrome, 182410 (3)	*CECR1*	2	30356112*
151	Xq21.1	X-LR	Occipital horn syndrome, 304150 (3); Menkes disease, 309400 (3); Spinal muscular atrophy, distal, X-linked 3, 300489 (3)	*ATP7A*	2	30356112*
152	Xp11.4	X-LR	Ornithine transcarbamylase deficiency, 311250 (3)	*OTC*	2	30356112*
153	Xq22.1	X-L	Fabry disease, 301500 (3); Fabry disease, cardiac variant, 301500 (3)	*GLA*	2	30356112*
154	Xq28	X-LR	Moyamoya disease 4, 300845 (4),	*MYMY4*	2	30356112*

155	Xq28	X-LR	NA	*F8A*	2	30356112*

Category: 1.1: Gene variations related to vascular risk factors: Hypertension; Category 1.2: Gene variations related to vascular risk factors: dyslipidemia; Category 1.3: Gene variations related to vascular risk factors: diabetes; Category 2: Gene variations related to other stroke subtypes.
*: stroke gene panel 1 (SGP1) from the article (PMID: 30356112), "genes were included that contain at least one variant for which a causative role has been shown or postulated and reported from at least one well-documented human patient in the literature"

eTable 2. Primers for the SNVs/ InDels and the balanced translocation validation by Sanger sequencing

Coordinate	Variants	Forward (5'-3')	Reverse (5'-3')
chr17:78350324 T>A	RNF213:NM_001256071:exon52 :c.T13409A:p.F4470Y	AATGCAAGATCCTTT CACCTCCT	CTGTGAAATAACAA AGGGCAAGG
chr17:78360549 G>A	RNF213:NM_001256071:exon63 :c.G14780A:p.R4927Q	GTTTTCCACTGCTCC AACTGT	TTCACAACAGACAC ACCAAATGA
chr17:78346850 G>A	RNF213:NM_001256071:exon49 :c.G12827A:p.R4276Q	GATGTGTTTCTGTGA ATGCCTGT	CTTCTCACCTGCTG CTTGACAA
chr17:78298836 A>G	RNF213:NM_001256071:exon18 :c.A3031G:p.T1011A	AAGGAAGGAGGGTG ACTGGTTAT	CGCAAACATACCAC ACAATCTGA
chr17:78332222 T>C	RNF213:NM_001256071:exon37 :c.T10997C:p.M3666T	TGTCGCTGTAGTGTG GTAAATAG	GCATATTAGGGTCC TGCTGTGTT
chr17:78360097 G>A	RNF213:NM_001256071:exon62 :c.G14587A:p.D4863N	GCATCAAAAGGGAG CTGAAAG	GCTGAAGGAGTGA GTGTCTGTT
chr17:78360619 G>C	RNF213:NM_001256071:exon63 :c.G14850C:p.E4950D	CCCTGCAACATAGAG CCCTAG	GAGGGAGGAGATA CAGACCAGA
chr17:78363034 C>T	RNF213:NM_001256071:exon65 :c.C15062T:p.A5021V	CGATTTGTTCCTGCT CTCCG	CCCTGAATGCTCCT ATCCCTC
chr17:78286895 G>A	RNF213:NM_001256071:exon15 :c.G2739A:p.W913X	GAATGGAAGTGCTTT GGGAATGT	AATCACGATCAGTC ACATCCCTA
chr17:78313074 C>T	RNF213:NM_001256071:exon26 :c.C4907T:p.T1636M	ACAATGACTCTTTCC CTGATGAG	CTTCTGGGTCACAA ATCTCTTCC
chr17:78320498 G>A	RNF213:NM_001256071:exon29 :c.G8363A:p.G2788D	TTCTGGATGAAATAA CACGGGC	CTCATCTAACACCA CCACAGAGA
chr17:78268635 G>A	RNF213:NM_001256071:exon9: c.G1588A:p.A530T	TCTGCCCCATTTACT CCATATCT	TCTTTCTCCCTGTAC TGCAAATC
chr17:78343634 G>A	RNF213:NM_001256071:exon46 :c.G12392A:p.R4131H	CAGAGTAGGTTGCTT TCTTCCTG	CACAACCAGTACAA GTAACCAGG
chr12:992685 G>A	WNK1:NM_018979:exon16:c.G 3614A:p.G1205E	ACCCAACCTGTGATT TAGTGATG	ACATAAAAGTTTGT TGTCGGTCA
chr12:988932 C>A	WNK1:NM_018979:exon11:c.C 2567A:p.T856K	GTACCAACTATCCAA GGCGAAC	GAAGCTGACTAGGA ACCACAGT
chr12:1009690 C>T	WNK1:NM_018979:exon26:c.C 6497T:p.T2166I	AACACCCAGCCTATC TATTGAGT	AGAAAGGCTTGGTA CTGAAATGG
chr17:40939485 C>A	WNK4:NM_032387:exon7:c.C1 666A:p.P556T	TGGTTTTCTTCCTCCC ATATCCT	GTCTCAAGATCAGG GGTGACTTA
chr12:20522382 T>C	PDE3A:NM_000921:exon1:c.T1 64C:p.L55P	AAACTTTCAGTGGAT TGTGGGC	AGAAGAAGGCACA CAGGAGAC
chr2:21225713 A>G	APOB:NM_000384:exon29:c.T1 2581C:p.I4194T	CCTCTTGGGCTTCTTT TGATAAA	TTGATGATATCGAC GTGAGGTTC
chr2:21263905 C>A	APOB:NM_000384:exon4:c.G28 8T:p.Q96H	ACAAATACTTACAGT CACATCCGT	TTGATAAGGCATGT GGTGTTGAG
chr2:21255236 C>T	APOB:NM_000384:exon10:c.G1 342A:p.A448T	ATGCAAGCTGTAATA CTTAGGGG	CCTTCTGATAGATG TGGTCACCT
chr2:21229376 G>A	APOB:NM_000384:exon26:c.C1 0364T:p.S3455F	GAGGGAATATATGCG TTGGAGTG	GTGGAGGGTAGTCA TAACAGTACT
chr2:21234872 C>T	APOB:NM_000384:exon26:c.G4 868A:p.G1623D	ACTGAATTTTGCATT GTGTTCCC	TTTGCCACTTCTAA CAAGATGGA
chr19:45411025 G>A	APOE:NM_000041:exon3:c.G52 A:p.A18T	CCACCATGGCTCCAA AGAAG	GTAATCCCAAAAGC GACCCAG
chr19:11224014 G>A	LDLR:NM_000527:exon9:c.G12 47A:p.R416Q	CTAGCCTCAAGTGAT CCTCCTC	CAGTAGATTCTATT GCTGGCCAC
chr19:11221444 G>A	LDLR:NM_000527:exon7:c.G10 57A:p.E353K	AATTAGCCTGTCATG GTCGTGG	ATGCAGGTGGAATC TCATGAAAC
chr1:55509520 C>A	PCSK9:NM_174936:exon2:c.C2 12A:p.P71Q	CAGAGGAAAACCTGT TGTCGAG	TCGCCACTCATCTT CACCAG
chr12:12334098 A>G	LRP6:NM_002336.2:exon1:c.T1 252C:p.Y418H	AGTAGAGCTTCTTAC CCAACCAT	ACTGGACTGATGAT GAAGTGAGG

chr12:12397399 T>A	LRP6:NM_002336:exon2:c.A246T:p.K82N	CCACTTGAAGGATCT AAGGCAAT	CTGCGGTGGACTTT GTGTTTAG
chr2:27721143 G>A	GCKR:NM_001486:exon4:c.G307A:p.V103M	TAGTGGAGCAAGAC ATGGGAG	CAACATACTGGCGG GACTCA
chr2: 27721171 G>A	GCKR:NM_001486:exon4:c.G335A:p.R112Q	TTGAACAAGTAGTGG AGCAAGAC	ATGGAATCTCGCAC TTAAAGCTG
chr11:11670713 6 T>C	APOA1: NM_000039:exon4:c.201-9A>G	ATCTCCTCCTGCCAC TTCTTC	AGGGGTGTTGGTTG AGAGTG
chr15:58837953 C>T	LIPC:NM_000236:exon5:c.C587T:p.A196V	TGTCATTGTTAGCAC CATGAACT	TAGTGTCCTATGGG CTGTTTGAT
chr20:43043159 G>A	HNF4A:NM_175914:exon5:c.G439A:p.V147I	AGACTCCTTGGGGCT CTAAAG	CACGGCTATATCCC AGGTGG
chr20:43043143 G>A	HNF4A:NM_175914:exon5:c.427-4G>A	TGCCTCATTGTCAGA AAAGGATG	TAAAATCAAGCCAG TCCACGG
chr20:43043127 C>T	HNF4A:NM_175914:exon5:c.427-20C>T	GCCTCATTGTCAGAA AAGGATGA	CTTCATGGACTCAC ACACATCTG
chr17:36093774 G>T	HNF1B:NM_000458:exon3:c.C585A:p.D195E	GTGTTACCTGTTGCA TTCCTCC	AAGCTTAGTTAGAC GAGGGGAAT
chr3:57286319 A>G	APPL1:NM_012096:exon12:c.A1075G:p.S359G	AAAGTCTGCATCCTG ATACCTCT	TTGCTCGAGGACAA TAGACTTTT
chr3:57293081 G>A	APPL1:NM_012096:exon16:c.G1456A:p.G486R	ATTGATCAGTTAGTG TGTGAGGG	TATGCTCCAGTACC AGAAGAGAA
chr9:135945901 A>G	CEL:NM_001807:exon10:c.A1349G:p.Y450C	AAGCCCCATCTCTTC ATGTGAA	CCCGAAAACGTACT GAATGTCAT
chr9:135944184 G>A	CEL:NM_001807:exon8:c.G1030A:p.G344S	CCCAAGTGTCCATAG ATCAGAGA	CTGCTTACTCCGTG ACTTTCTTG
chr12:12143411 7 C>A	HNF1A:NM_000545:exon5:c.C1008A:p.S336R	TTGGCAAAAGGTAGA AACAAAGG	AGGAAAGATGAGG TTGGGTTTTC
chr20:43043165 G>A	HNF4A:NM_175914:exon5:c.G445A:p.G149R	TGACAGACTCCTTGG GGCTC	CACTACTGCCCACC ATCCAC
chr3:12447429 C>T	PPARG:NM_005037:exon5:c.C584T:p.A195V	GATGGTCTGTGCTAC TTTTGTGA	GTCTGTTGTCTTTCC TGTCAAGA
chr19:15302649 C>T	NOTCH3:NM_000435:exon5:c.G709A:p.V237M	AGCCATTGACACACA CGCAG	CACCCTCACCATGC CGTAAC
chr19:15298126 G>A	NOTCH3:NM_000435:exon11:c.C1630T:p.R544C	CACTAGATGCACCAT TCCCAAA	CAAATTCTGGAGCT TGTAGTGGG
chr19:15285063 G>T	NOTCH3:NM_000435:exon25:c.C4552A:p.L1518M	ATGAAACACACAAG ACCTGGATC	GTACTCTACGGTGT GAATGCATG
chr19:15298066 C>T	NOTCH3:NM_000435:exon11:c.G1690A:p.A564T	CCACTAGATGCACCA TTCCCA	GTGGAGTGGAAGTA AGTGGGG
chr19:15276215 C>T	NOTCH3:NM_000435:exon31:c.G5779A:p.A1927T	ACTAGTGGTGACCCT GCATG	AACCGCTCTACAGA CTTGGATG
chr19:15289985 C>T	NOTCH3:NM_000435:exon22:c.G3569A:p.R1190H	AGCATGTAGATCAGC CACAATG	TCTTCATTCCCTCTT GACCACC
chr19:15295229 C>T	NOTCH3:NM_000435:exon16:c.G2443A:p.A815T	AGGCACACAGTTCAA GCTTAATG	TTATTTTGCCTTCAC CCATCTCG
chr 17:29548962 ->T	NF1:NM_001128147:exon15:c.1737dupT:p.Y579fs	TGATTTCATTCTGTCT GTATTATTCCC	TCATTCATCGAAAG CATTGGTATT
chrX:100658972 C>G	GLA:NM_000169:exon2:c.G196C:p.E66Q	AGTCCTCTGAATGAA CAAGAACAT	GGGCGGGAATATTA ACGGGAT
chr13:11116446 7 G>A	COL4A2:NM_001846:exon48:c.G5068A:p.A1690T	TTCATCGAATGCAAT GGAGGC	ATTGGAAAGTGCAG TGGTTACAT
chr13:11085088 9 G>T	COL4A1:NM_001845:exon21:c.C1210A:p.P404T	TCCACGCCTTTCTATT ACACTCT	CAGTGATGGTCTGG TTGGATTTT
chr13:11111792 0 C>T	COL4A2:NM_001846:exon25:c.C1945T:p.P649S	GAAAGGAAACAGGG AAGTCGAG	CAAAACAGCATCCT CATCTGACT
chr13:11107733 5 T>A	COL4A2:NM_001846:exon6:c.T351A:p.D117E	GAGACAAGGGTGAA AGGGGAG	TACGCACGTATAGT CCCCAC
chr13:11114208 3 A>C	COL4A2:NM_001846:exon36:c.A3297C:p.L1099F	CATGTGAGCCAATTT CAGACCT	TTCTTGCACATTGG ACTTGAAGA

	chr13:111111172 C>T	COL4A2:NM_001846:exon22:c.C1487T:p.P496L	GTCATAGTGCCCATCAGAACAG	GAGATAAAAGGCAAGAACGGGAC
	46,XY,t(15;22)(q24.2;q13.1)	der(15)	GATCACCTAGTTCACATCGCCA	GCTGATACCCTGGCTTTGC
	46,XY,t(15;22)(q24.2;q13.1)	der(22)	CGACGCTTCCTTAACACCAAAA	AACTGGGCATGTGGTTAAAGAC

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eTable 3. Frequency in public databases and prediction results of 59 rare SNVs and InDels

No.	Subject No.	Coordinate	Variants	Allele frequency in 92 patients	Category #	MAF in ChinaMAP	MAF in GnomAD EAS	MAF in European population from GnomAD	MAF in NCVD	SIFT	Polyphen 2 HVAR	Mutation Taster	CADD_phred	Reported	Remarks
1	IS0025F	chr12: 9926855 G>A	WNK1:NM_018979:exon16:c.G3614A:p.G1205E	1/184	1.1	9.44465E-05	0.000543656	0	0.000500167	damaging	possibly damaging	disease_causing	21.3	No	NA
2	IS0025F	chr12: 988932 C>A	WNK1:NM_018979:exon11:c.C2567A:p.T856K	1/184	1.1	0.000944465	0.001002506	0	0.001167056	tolerated	possibly damaging	disease_causing	23.2	No	NA
3	IS0025F	chr12: 20522382 T>C	PDE3A:NM_000921:exon1:c.T164C:p.L55P	1/184	1.1	9.44465E-05	8.67303E-05	0	NA	damaging	benign	disease_causing	18.33	No	NA
4	IS0099F	chr12: 10096990 C>T	WNK1:NM_018979:exon26:c.C6497T:p.T2166I	1/184	1.1	0.001086135	0.000326193	0	0.000833611	damaging	possibly damaging	disease_causing	28.2	No	NA
5	ISP0019F, IS0039F	chr17: 40939485 C>A	WNK4:NM_032387:exon7:c.C1666A:p.P556T	2/184	1.1	0.005289006	0.00491573	5.19798E-05	NA	tolerated	benign	polymorphism	0.005	Yes, PMID: 15110905	P556T variant was identified in two Japanese patients with hypertension or renal failure
6	ISP0026F	chr2:212257 13 A>G	APOB:NM_000384:exon29:c.T12581C:p.I4194T	1/184	1.2	0.003777862	0.001555288	3.91676E-05	0.003834612	damaging	benign	polymorphism	7.556	Yes, PMID: 27932355	I4194T is a specific familial hypercholesterolemia mutation predicted in silico analysis
7	IS0016F	chr2:212639 05 C>A	APOB:NM_000384:exon4:c.G288T:p.Q96H	1/184	1.2	0.005714016	0.006117128	0	0.006335445	tolerated	benign	disease_causing	23.9	Yes, PMID: 27932355	Q96H is a specific familial hypercholesterolemia mutation predicted in silico analysis
8	IS0033F	chr2:212552 36 C>T	APOB:NM_000384:exon10:c.G1342A:p.A448T	1/184	1.2	0.000330563	0.000272005	7.43915E-06	NA	tolerated	benign	polymorphism	21.3	Yes, PMID: 27932355	A448T is a specific familial hypercholesterolemia mutation

9	IS0122B	chr2:212293 76 G>A	APOB:NM_000384:exon26:c.C10364T:p.S3455F	1/184	1.2	NA	NA	NA	NA	damaging	damaging	disease_causing	23.4	No	predicted in silico analysis NA
10	IS0013F	chr2:212348 72 C>T	APOB:NM_000384:exon26:c.G4868A:p.G1623D	1/184	1.2	0.000188893	0.000271976	0	NA	tolerated	benign	disease_causing	23.6	No	NA
11	IS0079F	chr19:45411 025 G>A	APOE:NM_000041:exon3:c.G52A:p.A18T	1/184	1.2	0.001038912	0.002327464	0	0.000833611	damaging	benign	polymorphism	20.2	No	NA
12	IS0048F	chr19:11224 014 G>A	LDLR:NM_000527:exon9:c.G1247A:p.R416Q	1/184	1.2	4.72233E-05	5.01505E-05	2.59669E-05	NA	damaging	possibly damaging	disease_causing	26.4	Yes, PMID: 20506408, 22294733, 9452095, 15241806, 11810272	The R416Q (also known as R395Q) variant in LDLR has been reported in at least 84 individuals with Familial Hypercholesterolemia;Missense variants in the same codon (R416W, R416P, R416L) have been reported in the HGMD in association with familial hypercholesterolemia.
13	ISP0070F	chr19:11221 444 G>A	LDLR:NM_000527:exon7:c.G1057A:p.E353K	1/184	1.2	0.000188893	0.000350948	3.90997E-05	NA	tolerated	possibly damaging	disease_causing	23.1	Yes, PMID: 20506408; 16250003	E353K variant was referred from the cascade screening program for familial hypercholesterolemia.
14	IS0053F	chr1:555095 20 C>A	PCSK9:NM_174936:exon2:c.C212A:p.P71Q	1/184	1.2	4.72233E-05	NA	NA	NA	tolerated	benign	disease_causing	13.88	Yes, PMID: 26374825(same position, but not the	P71Q variant is in the same codon of P71L, which is the familial gain of funcion mutation.

														same variant)	
15	IS0012F	chr12:123340098A>G	LRP6:NM_002336.2:exon1:c.T1252C:p.Y418H	1/184	1.2	0.003258406	0.00491 2281	0	0.00333 4445	damaging	probably damaging	disease_causing	26	Yes, PMID: 27455246	Y418H variant is cosegregated the family with coronary artery disease and this variant significantly debilitated the Wnt3a-associated signaling pathway and impair the endothelial cell functions.
16	IS0025F, IS0050F, IS0103F	chr12:12397399T>A	LRP6:NM_002336:exon2:c.A246T:p.K82N	2/184	1.2	0.003258406	0.00410 9864	0	0.00450 1501	tolerated	benign	disease_causing	17.33	Yes, PMID: 24427284	The in vitro functional analysis revealed that K82N variant resulted in a significant reduction in both protein level transporting to cell membrane and downstream Wnt signal activity.
17	IS0003F	chr2:27721143G>A	GCKR:NM_001486:exon4:c.G307A:p.V103M	1/184	1.2	0.01010578	0.00862 5013	2.59306 E-05	0.00766 9223	damaging	probably damaging	disease_causing	23	Yes, PMID: 22182842	V103M variant is detected in the ClinSeq cohort and shows significantly reduced inhibition of glucokinase in vitro
18	IS0071F	chr2:27721171G>A	GCKR:NM_001486:exon4:c.G335A:p.R112Q	1/184	1.2	NA	5.01303 E-05	1.94542 E-05	NA	damaging	probably damaging	polymorphism	28.7	No	NA
19	IS0013F	chr11:116707136T>C	APOA1:NM_000039:exon4:c.201-9A>G,	1/184	1.2	0.000661126	0.00141 4427	0	0.00133 3778	-	-	-	-	No	NA

20	IS0011F	chr15:58837953 C>T	LIPC:NM_000236:exon5:c.C587T:p.A196V	1/184	1.2	NA	0.000100241	0	NA	damaging	probably damaging	disease_causing	29.1	No	NA
21	IS0016F, IS0145B, ISP0057B	chr20:43043159 G>A	HNF4A:NM_175914:exon5:c.G439A:p.V147I	3/184	1.3	0.003825085	0.00180415	0.000213977	0.002667556	tolerated	benign	polymorphism	5.767	Yes, PMID:15281001	HNF4A:NM_175914:exon5:c.G439A:p.V147I, c.426+703G>A and c.427-20C>T has been identified in a Philippino family with autosomal dominant early–onset type 2 diabetes and cosegregated with 3 affected available siblings, age of onset from 31 to 46
22	IS0016F, IS0145B, ISP0057B	chr20:43043143 G>A	HNF4A:NM_175914:exon5:c.427-4G>A	3/184	1.3	0.003777862	0.00175421	0.000149194	0.002667556	NA	NA	NA	NA	Yes, PMID:15281001	HNF4A:NM_175914:exon5:c.G439A:p.V147I, c.426+703G>A and c.427-20C>T has been identified in a Philippino family with autosomal dominant early–onset type 2 diabetes and cosegregated with 3 affected available siblings, age of onset from 31 to 46
23	IS0016F, IS0145B, ISP0057B	chr20:43043127 C>T	HNF4A:NM_175914:exon5:c.427-20C>T	3/184	1.3	0.003777862	0.00180433	0	0.002667556	NA	NA	NA	NA	Yes, PMID:15281001	HNF4A:NM_175914:exon5:c.G439A:p.V147I, c.426+703G>A and c.427-20C>T has been identified in a

															Philippino family with autosomal dominant early–onset type 2 diabetes and cosegregated with 3 affected available siblings, age of onset from 31 to 46
24	IS0027F	chr17:36093774 G>T	HNF1B:NM_000458:exon3:c.C585A:p.D195E	1/184	1.3	NA	0	7.38989E-06	NA	NA	probably damaging	disease_causing	13.92	No	NA
25	IS0025F	chr12:121434117 C>A	HNF1A:NM_000545:exon5:c.C1008A:p.S336R	1/184	1.3	4.72233E-05	0.000271887	0	0.000333444	tolerated	possibly damaging	disease_causing	21.8	No	NA
26	IS0103F	chr20:43043165 G>A	HNF4A:NM_175914:exon5:c.G445A:p.G149R	1/184	1.3	0.000188893	0.000200461	3.24179E-05	NA	tolerated	benign	disease_causing	24	no	NA
27	IS0024F	chr3:57286319 A>G	APPL1:NM_012096:exon12:c.A1075G:p.S359G	1/184	1.3	NA	NA	NA	NA	tolerated	benign	disease_causing	24.2	No	NA
28	IS0053F	chr3:57293081 G>A	APPL1:NM_012096:exon16:c.G1456A:p.G486R	1/184	1.3	NA	0.000218341	0	0.000166722	damaging	benign	disease_causing	23.3	No	NA
29	IS0013F	chr9:135945901 A>G	CEL:NM_001807:exon10:c.A1349G:p.Y450C	1/184	1.3	NA	0.000278118	2.22628E-05	NA	damaging	probably damaging	disease_causing	23.3	No	NA
30	IS0068F	chr9:135944184 G>A	CEL:NM_001807:exon8:c.G1030A:p.G344S	1/184	1.3	NA	NA	NA	NA	damaging	probably damaging	disease_causing	28.1	No	NA
31	ISP0063F	chr3:124474297 C>T	PPARG:NM_005037:exon5:c.C584T:p.A195V	1/184	1.3	NA	0.000163185	0	NA	damaging	possibly damaging	disease_causing	34	No	NA
32	IS0035F	chr19:15302649 C>T	NOTCH3:NM_000435:exon5:c.G709A:p.V237M	1/184	2	0.003825085	0.002356362	2.60335E-05	0.006335445	damaging	benign	disease_causing	26.7	Yes, PMID:12480761	NOTCH3: V237M variant was detected in a Japanese patient with CADASIL

33	IS0050F, IS0145B	chr19:15298126 G>A	NOTCH3:NM_000435:exon11:c.C1630T:p.R544C	2/184	2	0.000330563	0.00396666	0	0.000333444	tolerated	possibly damaging	disease_causing	24.7	Yes, PMID:10371548	NOTCH3 c.1630C>T (p.Arg544Cys) missense variant has been reported extensively in the literature, particularly in individuals affected with cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) of Asian descent, where the variant appears to be a founder variant
34	IS0007F, ISP0019F, ISP0023F	chr19:15285063 G>T	NOTCH3:NM_000435:exon25:c.C4552A:p.L1518M	3/184	2	0.007650893	0.006700702	0.00038111	0.008502834	damaging	probably damaging	disease_causing	27.8	Yes, PMID:22006983	NOTCH3 L1518M was predicted as functional but in small vessel disease patient
35	IS0047F	chr19:15298066 C>T	NOTCH3:NM_000435:exon11:c.G1690A:p.A564T	1/184	2	0.001180582	0.00125439	4.54734E-05	0.001000333	tolerated	probably damaging	disease_causing	27.8	No	NA
36	IS0028F	chr19:15276215 C>T	NOTCH3:NM_000435:exon31:c.G5779A:p.A1927T	1/184	2	0.000236116	0.000435019	2.27218E-05	0.001333778	tolerated	benign	disease_causing	23	No	NA
37	IS0044F	chr19:15289985 C>T	NOTCH3:NM_000435:exon22:c.G3569A:p.R1190H	1/184	2	9.44465E-05	0	6.51755E-06	NA	tolerated	probably damaging	disease_causing	24.3	No	NA
38	IS0106F	chr19:15295229 C>T	NOTCH3:NM_000435:exon16:c.G2443A:p.A815T	1/184	2	NA	0.000108814	0	NA	tolerated	benign	disease_causing	20.3	No	NA
39	IS0119F	chr17:29548962 ->T	NF1:NM_001128147:exon15:c.1737dupT:p.Y579fs	1/184	2	NA	0.000699526	0	0.000333444	-	-	-	-	No	NA

40	IS0059F	chrX:100658972 C>G	GLA:NM_000169:exon2:c.G196C:p.E66Q	1/184	2	NA	0.001479987	0	NA	damaging	possibly damaging	disease_causing	25.4	Yes, PMID: 1315715;26456105	Peng et al. suggested that the GLA E66Q vairnat could be one of the genetic causes of the Chinese renal variant FD pedigree.
41	IS0004F	chr13:111164467 G>A	COL4A2:NM_001846:exon48:c.G5068A:p.A1690T	1/184	2	0.000897242	0.001998565	3.26426E-05	0.001000333	damaging	possibly damaging	polymorphism	22.8	Yes, PMID: 22209247	COL4A2 p.A1690T variant was found in a intracerebral hemorrhage patient. This mutation can cause expense of their secretion.
42	IS0152B	chr13:110850889 G>T	COL4A1:NM_001845:exon21:c.C1210A:p.P404T	1/184	2	NA	0.000163221	0	NA	tolerated	possibly damaging	disease_causing	15.13	No	NA
43	IS0017F; IS0060F; ISP0026F	chr13:111117920 C>T	COL4A2:NM_001846:exon25:c.C1945T:p.P649S	3/184	2	0.001038912	0.002052545	0	0.001167056	tolerated	probably damaging	disease_causing	19.57	No	NA
44	IS0058	chr13:111077335 T>A	COL4A2:NM_001846:exon6:c.T351A:p.D117E	1/184	2	NA	5.56235E-05	0	NA	tolerated	probably damaging	disease_causing	26.6	No	NA
45	IS0068F	chr13:111142083 A>C	COL4A2:NM_001846:exon36:c.A3297C:p.L1099F	1/184	2	0.000425009	0.000445087	0	0.000333444	damaging	probably damaging	disease_causing	9.484	No	NA
46	IS0084F	chr13:111111172 C>T	COL4A2:NM_001846:exon22:c.C1487T:p.P496L	1/184	2	0.000519456	0.000871259	0	0.000333444	damaging	probably damaging	disease_causing	26.9	No	NA
47	IS0021F	chr17:78350324 T>A	RNF213:NM_001256071:exon52:c.T13409A:p.F4470Y	1/184	2	9.44465E-05	0.000271828	0	0.000333444	tolerated	probably damaging	polymorphism	25.2	No	NA
48	IS0024F	chr17:78360549 G>A	RNF213:NM_001256071:exon63:c.G14780A:p.R4927Q	1/184	2	0.000330563	0.000250652	8.4281E-05	NA	tolerated	benign	polymorphism	25.3	Yes, PMID: 25964206; 30671466	R4927Q is a rare missense variant in Japanese Moyamoya disease patients

49	IS0027F	chr17:78346850 G>A	RNF213:NM_001256071:exon49:c.G12827A:p.R4276Q	1/184	2	4.72233E-05	0	3.24958E-05	NA	tolerated	possibly damaging	polymorphism	25	No	NA
50	IS0028F	chr17:78298836 A>G	RNF213:NM_001256071:exon18:c.A3031G:p.T1011A	1/184	2	NA	NA	NA	NA	damaging	possibly damaging	polymorphism	12.36	No	NA
51	IS0039F	chr17:78332222 T>C	RNF213:NM_001256071:exon37:c.T10997C:p.M3666T	1/184	2	0.00273895	0.004410143	0	0.002334111	damaging	probably damaging	disease_causing	27.3	Yes, PMID: 26530418; 27128593	M3666T is a rare missense variant detected in Chinese Moyamoya disease patients
52	IS0042F	chr17:78360097 G>A	RNF213:NM_001256071:exon62:c.G14587A:p.D4863N	1/184	2	0.002219494	0.0008529	0	0.001833945	tolerated	benign	polymorphism	23	Yes, PMID: 21799892, 29160859, 30925911	D4863N is paticulaly identified in Chinese Moyamoya disease patients. This variant also significantly associated with intracranial major artery stenosis/occlusion.
53	IS0051F; IS0110B	chr17:78360619 G>C	RNF213:NM_001256071:exon63:c.G14850C:p.E4950D	2/184	2	0.002786173	0.002656642	0	0.002167389	tolerated	benign	polymorphism	12.41	Yes, PMID: 21799892, 29165161; 30925911	E4950D is paticulaly identified in Chinese Moyamoya disease patients. This variant also significantly associated with intracranial major artery stenosis/occlusion.
54	IS0141B	chr17:78363034 C>T	RNF213:NM_001256071:exon65:c.C15062T:p.A5021V	1/184	2	0.008311296	0.004259798	0	0.004001334	tolerated	benign	polymorphism	13.23	Yes, PMID: 29165161; 30925911	A5021V is significantly associated with MMD in Chinese population in the pooled analysis.
55	IS0049F	chr17:78286	RNF213:NM_001256071:exon15:c.G2739A:p.W913X	1/184	2	NA	NA	NA	NA	-	-	-	35	No	NA

		895 G>A													
56	IS0071F	chr17:78313074 C>T	RNF213:NM_001256071:exon26:c.C4907T:p.T1636M	1/184	2	NA	9.41265E-05	3.20605E-05	NA	damaging	-	polymorphism	22.1	No	NA
57	IS0147B	chr17:78320498 G>A	RNF213:NM_001256071:exon29:c.G8363A:p.G2788D	1/184	2	NA	NA	NA	NA	damaging	possibly damaging	disease_causing	24.3	No	NA
58	ISP0009F	chr17:78268635 G>A	RNF213:NM_001256071:exon9:c.G1588A:p.A530T	1/184	2	NA	0	2.95425E-05	NA	damaging	possibly damaging	polymorphism	17.82	No	NA
59	ISP0057B	chr17:78343634 G>A	RNF213:NM_001256071:exon46:c.G12392A:p.R4131H	1/184	2	NA	0	2.96314E-05	NA	damaging	probably damaging	disease_causing	35	No	NA

MAF: Minor allele frequency
ChinaMAP: Chinese subjects with metabolic traits and diseases
NCVD: Nyuwa Chinese Population Variant Database
#Category 1.1: Gene variations related to vascular risk factors: Hypertension; Category 1.2: Gene variations related to vascular risk factors: dyslipidemia; Category 1.3: Gene variations related to vascular risk factors: diabetes; Category 2: Gene variations related to other stroke subtypes.

eTable 4. The VRFs profile for patients with VRFs-related variants

Study No	Sex	Age at onset of stroke	Diabetes#	Diabetes related variants	Hypertension#	Hypertension related variants	Dyslipidemia#	Dyslipidemia related variants	VRF-related variants	Consistency of Genetic Results with the Baseline Assessment for VRFs
IS0003F	Male	59	No	No	No	No	Yes*	Yes*	GCKR:NM_001486:exon4:c.G307A:p.V103M	Y
IS0011F	Female	65	No	No	Yes	No	Yes*	Yes*	LIPC:NM_000236:exon5:c.C587T:p.A196V	Y
IS0012F	Male	58	No	No	Yes	No	Yes*	Yes*	LRP6:NM_002336.2:exon1:c.T1252C:p.Y418H	Y
IS0013F	Female	71	No	Yes	No	No	Yes*	Yes*	APOB:NM_000384:exon26:c.G4868A:p.G1623D APOA1: NM_000039:exon4:c.201-9A>G CEL:NM_001807:exon10:c.A1349G:p.Y450C	N,P
IS0016F	Male	68	No	Yes	Yes	No	Yes*	Yes*	APOB:NM_000384:exon4:c.G288T:p.Q96H HNF4A:NM_175914:exon5:c.G439A:p.V147I HNF4A:NM_175914:exon5:c.427-4G>A HNF4A:NM_175914:exon5:c.427-20C>T	N,P
IS0024F	Male	55	No	Yes	Yes	No	Yes	No	APPL1:NM_012096:exon12:c.A1075G:p.S359G	N
IS0025F	Male	61	Yes*	Yes*	Yes*	Yes*	Yes*	Yes*	WNK1:NM_018979:exon16:c.G3614A:p.G1205E WNK1:NM_018979:exon11:c.C2567A:p.T856K PDE3A:NM_000921:exon1:c.T164C:p.L55P LRP6:NM_002336:exon2:c.A246T:p.K82N HNF1A:NM_000545:exon5:c.C1008A:p.S336R	Y
IS0027F	Female	54	Yes*	Yes*	Yes	No	Yes	No	HNF1B:NM_000458:exon3:c.C585A:p.D195E	Y
IS0033F	Male	65	No	No	No	No	No	Yes	APOB:NM_000384:exon10:c.G1342A:p.A448T	N

IS0039F	Male	75	No	No	No	Yes	No	No	WNK4:NM_032387:exon7:c.C1666A:p.P556T	N
IS0048F	Male	73	No	No	Yes	No	Yes*	Yes*	LDLR:NM_000527:exon9:c.G1247A:p.R416Q	Y
IS0050F	Male	79	Yes	No	Yes	No	Yes*	Yes*	LRP6:NM_002336:exon2:c.A246T:p.K82N	Y
IS0053F	Female	57	No	Yes	Yes	No	Yes*	Yes*	PCSK9:NM_174936:exon2:c.C212A:p.P71Q APPL1:NM_012096:exon16:c.G1456A:p.G486R	N,P
IS0068F	Male	54	No	Yes	Yes	No	No	No	CEL:NM_001807:exon8:c.G1030A:p.G344S	N
IS0071F	Male	49	Yes	No	Yes	No	No	Yes	GCKR:NM_001486:exon4:c.G335A:p.R112Q	N
IS0079F	Female	45	Yes	No	No	No	Yes*	Yes*	APOE:NM_000041:exon3:c.G52A:p.A18T	Y
IS0099F	Male	47	No	No	No	Yes	Yes	No	WNK1:NM_018979:exon26:c.C6497T:p.T2166I	N
IS0103F	Male	40	Yes*	Yes*	Yes	No	Yes*	Yes*	LRP6:NM_002336:exon2:c.A246T:p.K82N HNF4A:NM_175914:exon5:c.G445A:p.G149R	Y
IS0122B	Female	55	No	No	No	No	Yes*	Yes*	APOB:NM_000384:exon26:c.C10364T:p.S3455F	Y
IS0145B	Male	57	Yes*	Yes*	No	No	Yes	No	HNF4A:NM_175914:exon5:c.G439A:p.V147I HNF4A:NM_175914:exon5:c.427-4G>A HNF4A:NM_175914:exon5:c.427-20C>T	Y
ISP0019F	Male	75	Yes	No	Yes*	Yes*	Yes	No	WNK4:NM_032387:exon7:c.C1666A:p.P556T	Y
ISP0026F	Male	69	No	No	No	No	Yes*	Yes*	APOB:NM_000384:exon29:c.T12581C:p.I4194T	Y
ISP0057B	Male	62	Yes*	Yes*	Yes	No	Yes	No	HNF4A:NM_175914:exon5:c.G439A:p.V147I HNF4A:NM_175914:exon5:c.427-4G>A HNF4A:NM_175914:exon5:c.427-20C>T	Y
ISP0063F	Male	63	No	Yes	Yes	No	No	No	PPARG:NM_005037:exon5:c.C584T:p.A195V	N

ISP0070F	Female	64	No	No	Yes	No	Yes*	Yes*	LDLR:NM_000527:exon7:c.G1057A :p.E353K	Y

#: Y/N: The patient had or did not have this phenotype

*: The genotype which was consistent with the phenotype.

VRF: Vascular risk factors (Hypertension; Diabetes; Dyslipidemia)
^: Y: Yes; N: No; N,P: partially consistent

eTable 5. Rare aneuploidies /CNVs and structural rearrangements in eight symptomatic ICAD patients

Sample Name	Gender	Age at Stroke Onset	Hypertension#	Diabetes#	Dyslipidemia#	Variant*
ISP0026F	Male	69	N	N	Y	seq[GCRh37] del(10)(10q11.22q11.23) chr10:g.46582529_51595727del
IS0016F	Male	68	Y	N	Y	seq[GCRh37] mos del(2)(p23.3) chr2:g.25251700_26670643del;
IS0004F	Male	69	Y	Y	Y	45,X/46,XY (50%)
IS0032F	Male	64	Y	N	Y	45,X/46,XY (15.4%)
IS0060F	Male	69	Y	Y	N	45,X/46,XY (12.5%)
ISP0019F	Male	75	Y	Y	Y	45,X/46,XY (22.4%)
ISP0036F	Male	67	Y	Y	Y	45,X/46,XY (19.1%)
IS0003F	Male	59	N	N	Y	seq[GCRh37] 46,XY,t(15;22)(q24.2;q13.1), der(15)(15pter->15q24.2(76,503,998)::TCACTG::22q13.1(39,580,634)->22qter),der(22)(22pter->22q13.1(39,580,63{1-2})::15q24.2(76,503,99{6-7})->15qter)

#Y/N: The patient had or did not have this phenotype
*Description of variants follows the International Soceity of Cytogenomic Nomenclature (ISCN) 2016

eTable 6.Other CNVs and structural rearrangements detected in this cohort

Sample Name	Gender	Age at onset of stroke	Hypertension#	Diabetes#	Dyslipidemia#	Variants
IS0016F	Male	68	Y	N	Y	seq[GCRh37] mos del(2)(q12.2q13) chr2:g.106578814_111586107del seq[GCRh37] mos del(16)(q24.2q24.3) chr16:g.88015252_89439554del
IS0004F	Male	69	N	Y	Y	seq[GCRh37] ins(21;21)(q22.11;q22.11)(pter->q22.11(+)(31787784):TGTA:q22.11(-)(31759988)<- q22.11(-)(31748571)::q22.11(+)(31772144)->qter) dup(21)(q22.11) chr21:g.31748571_31759988dup dup(21)(q22.11) chr21:g.31772144_31787784dup
IS0038F	Male	68	Y	N	Y	seq[GCRh37] ins(14;14)(q21.3;q21.3)(pter->q21.3(+)(4850885[16])::q21.3(-)(4847995[16])<- q21.3(-)(48464141)::q21.3(+)(48483961)->qter) dup(14)(q21.3) chr14:g.48464141_48479953dup dup(14)(q21.3) chr14:g.48483961_48508853dup
IS0141B	Male	48	N	N	Y	seq[GCRh37] ins(14;14)(q21.3;q21.3)(pter->q21.3(+)(4850885[16])::q21.3(-)(4847995[16])<- q21.3(-)(48464141)::q21.3(+)(48483961)->qter) dup(14)(q21.3) chr14:g.48464141_48479953dup dup(14)(q21.3) chr14:g.48483961_48508853dup

#: Y/N: The patient had or did not have this phenotype

eTable 7. Gene enrichment analysis for the candidate variants involved genes.

GO	Category	Description	Count	Log10 (P)	Log10 (q)
GO:0030301	GO Biological Processes	cholesterol transport	9	-14.93	-10.56
GO:0055090	GO Biological Processes	acylglycerol homeostasis	5	-9.34	-6.36
M106	Canonical Pathways	PID HNF3B PATHWA	5	-9.19	-6.25
GO:0001568	GO Biological Processes	blood vessel development	10	-8.91	-5.99
GO:0072001	GO Biological Processes	renal system development	7	-7.94	-5.1
GO:0090118	GO Biological Processes	receptor-mediated endocytosis involved in cholesterol transport	3	-7.36	-4.66
GO:0030157	GO Biological Processes	pancreatic juice secretion	3	-6.76	-4.2
GO:0007369	GO Biological Processes	gastrulation	5	-6.07	-3.67
GO:0071363	GO Biological Processes	cellular response to growth factor stimulus	7	-5.53	-3.23
WP363	WikiPathways	Wnt signaling pathway	3	-4.75	-2.57

WP4239	WikiPathways	Epithelial to mesenchymal transition in colorectal cancer	4	-4.75	-2.57
hsa00561	KEGG Pathway	Glycerolipid metabolism	3	-4.61	-2.46
GO:0071417	GO Biological Processes	cellular response to organonitrogen compound	6	-4.59	-2.45
GO:0019221	GO Biological Processes	cytokine-mediated signaling pathway	5	-4.11	-2.03

Log10(P)" is the p-value in log base 10. "Log10(q)" is the multi-test adjusted p-value in log base 10.