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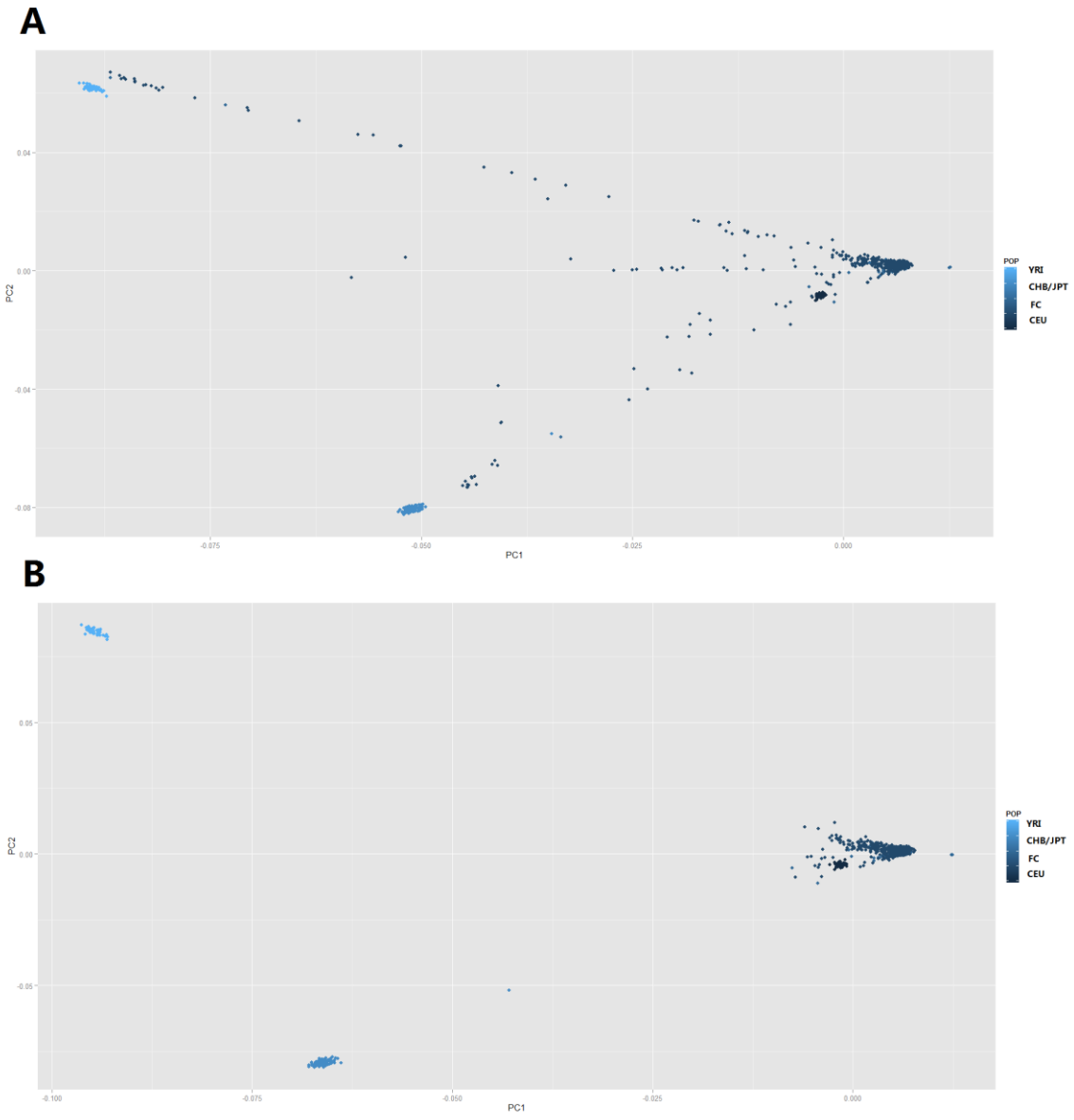
Supplemental Data

RNF213 Is Associated with Intracranial Aneurysms in the French-Canadian Population

Sirui Zhou, Amirthagowri Ambalavanan, Daniel Rochefort, Pingxing Xie, Cynthia V. Bourassa, Pascale Hince, Alexandre Dionne-Laporte, Dan Spiegelman, Ziv Gan-Or, Cathy Mirarchi, Vessela Zaharieva, Nicolas Dupré, Hatasu Kobayashi, Toshiaki Hitomi, Kouji Harada, Akio Koizumi, Lan Xiong, Patrick A. Dion, and Guy A. Rouleau

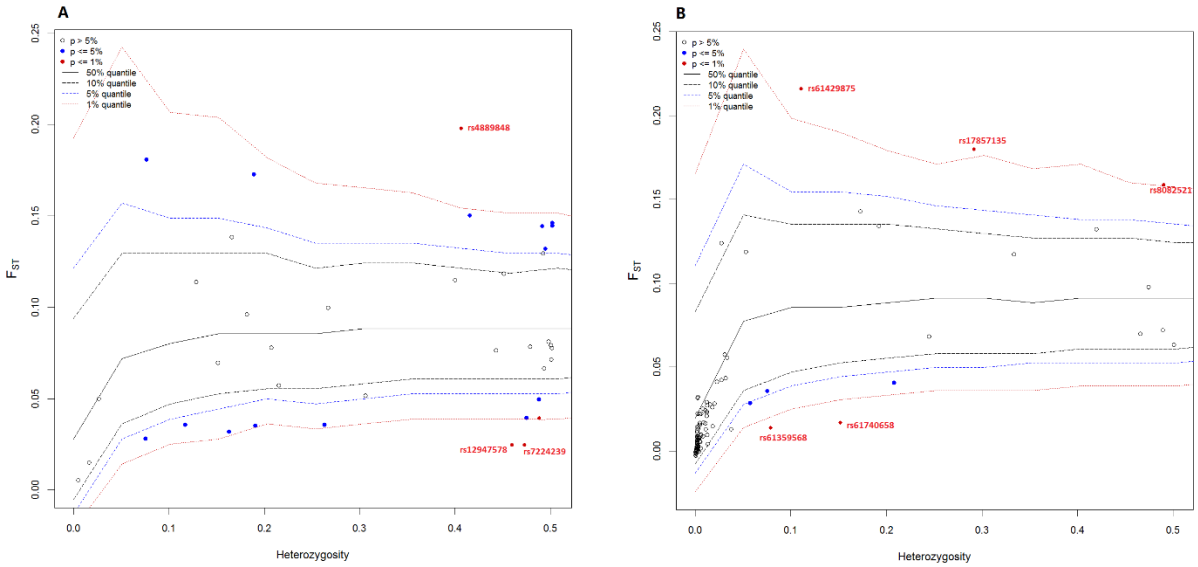
Figure S1: PCA analysis of FC patients and controls



PCA analysis done using smartPCA and graph constructed by R. (A) PCA plot of the FC NeuroX cohort (B) Samples involved in this study after the removal of 95 admixed individuals. YRI, CHB/JPT and CEU

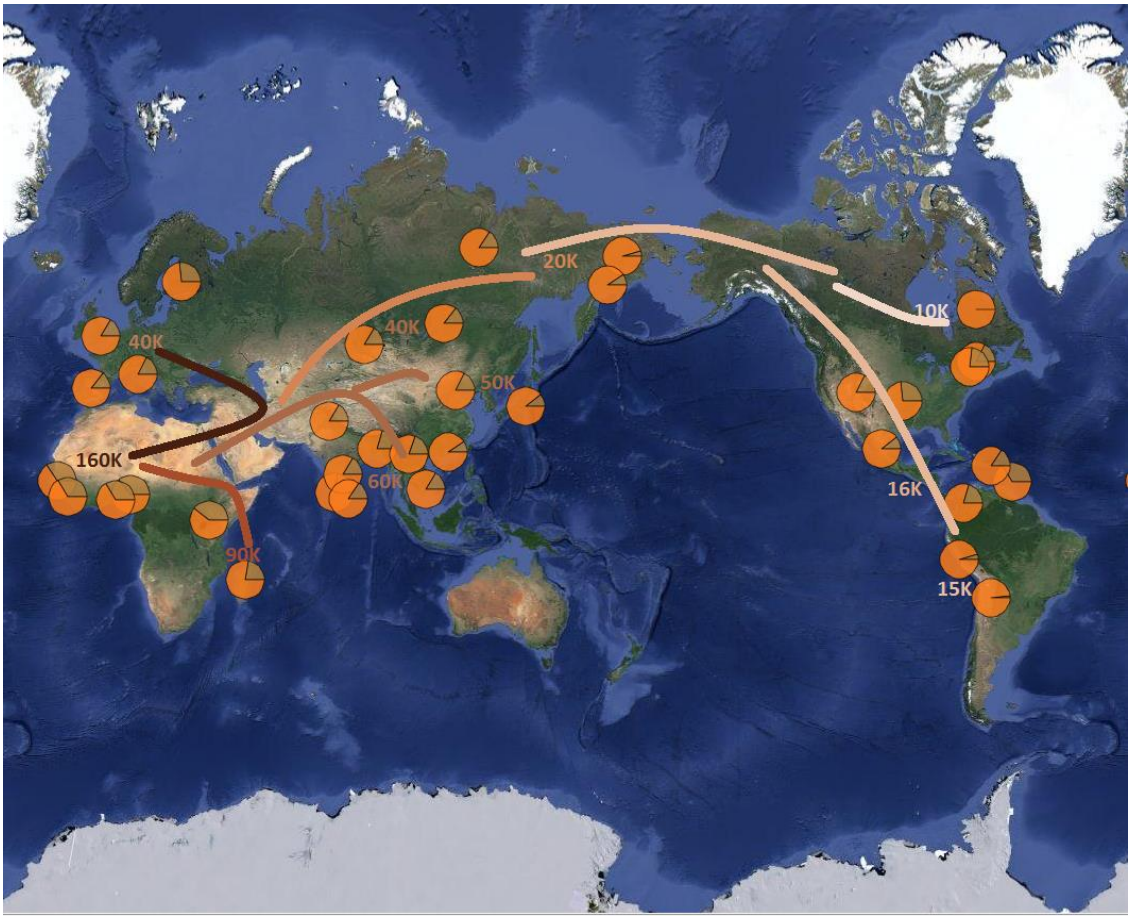
populations from 1KG phase III were used for clustering and outliers with less than 90% of European ancestry are removed.

Figure S2: *F*st of *RNF213* common variations between worldwide populations



F_{ST} of RNF213 common variants (A) and (B) functional variants, SNPs in red indicate they are outliers of 50% quantile.

Figure S3: MAF of rs6565666 distribution in world-wide populations



The frequency of rs6565666 non-ancestral allele decreased from Africans (0.26-0.35) to Europeans (0.16-0.18) and Asians (0.17-0.1) to the lowest in arctic populations (0.04-0.003). This non-ancestral allele seem also to be the risk allele for IA (dominant model for minor allele, p=0.0001739), which seems to correlate with the Out-of-Africa migration patterns and risk allele being purged in the evolution.

Table S1. Clinical descriptions of the IA discovery cohort and replication cohort.

	Number of individuals in discovery cohort	Number of individuals in replication cohort (familial)	Number of individuals in replication cohort (sporadic)
With clinical file	26	147	65
Multiple aneurysms	12	55	19
SAH	5	51	25
Hypertension	4	60	31
Drinking	12	33	26
Smoking	24	89	50
Hypercholesterolemia	3	29	24
Hypothyroidism	0	17	14
Had heart diseases and other vascular diseases	0	13	3

Table S3: Population data retrieved for this study

Region	**Populations**	**No. Samples**	**Data access**	**Data source**	**SNPs in RNF213**
Argentina	Argentina	50	GEO	Omni	40
Siberia	Chukotka	48	GEO	Omni	48
Siberia	East-Siberia	85	GEO	Omni	48
Kamchatka Krai	Kamchatka Krai	67	GEO	Omni	48
Sakha Republic	Sakha Republic	46	GEO	Omni	48
West-Siberia	West-Siberia	103	GEO	Omni	48
Africa	Madagascar	69	GEO	Omni	39
East_Asia	Han Chinese	203	1000 Genome	Omni & Exome	1835
East_Asia	JPT	104	1000 Genome	Omni & Exome	1835
East_Asia	CDX	93	1000 Genome	Omni & Exome	1835
East_Asia	Vietnamese	117	1000 Genome & GEO	Omni & Exome	1835
Europe	CEU	99	1000 Genome	Omni & Exome	1835

Europe	TSI	107	1000 Genome	Omni & Exome	1835
Europe	GBR	91	1000 Genome	Omni & Exome	1835
Europe	FIN	99	1000 Genome	Omni & Exome	1835
Europe	IBS	107	1000 Genome	Omni & Exome	1835
Africa	YRI	108	1000 Genome	Omni & Exome	1835
Africa	LWK	99	1000 Genome	Omni & Exome	1835
Africa	GWD	113	1000 Genome	Omni & Exome	1835
Africa	MSL	85	1000 Genome	Omni & Exome	1835
Africa	ESN	99	1000 Genome	Omni & Exome	1835
Native-America	ASW	61	1000 Genome	Omni & Exome	1835
Native-America	ACB	96	1000 Genome	Omni & Exome	1835
Native-America	MXL	64	1000 Genome	Omni & Exome	1835
Native-America	PUR	104	1000 Genome	Omni & Exome	1835
Native-America	CLM	94	1000 Genome	Omni & Exome	1835
Native-America	PEL	85	1000 Genome	Omni & Exome	1835
South_Asia	GIH	103	1000 Genome	Omni & Exome	1835
South_Asia	PJL	96	1000 Genome	Omni & Exome	1835
South_Asia	BEB	86	1000 Genome	Omni & Exome	1835
South_Asia	STU	102	1000 Genome	Omni & Exome	1835
South_Asia	ITU	102	1000 Genome	Omni & Exome	1835
Inuit	Inuit	185	In house & GEO	Omni	39

Table S4: Exome sequencing coverage of 26 IA patients from the initial cohort

Indiv	**Raw reads**	**% Coverage (10X)**	**20X**	**30X**	**50X**	**75X**	**100X**	**Average base depth**
09-1	7.90E+07	97.1	90.7	81.2	59.8	35.5	18.5	66.07
09-2	8.80E+07	97.8	93.6	86.5	68.4	46.1	28.1	78.44
28-1	1.40E+08	98.4	97	94.7	87.5	75.8	63.4	144.4

28-2	1.40E+08	98.7	97.1	94.3	85.8	72.8	59.5	133.63
28-3	1.04E+08	98.2	95.6	90.9	77.7	59.5	42.6	99.55
28-4	9.10E+07	98.2	95	89.5	75	55.8	38.7	93.58
94-1	1.10E+08	98.5	96.7	93.3	82.4	65.7	49.7	111.25
94-2	1.10E+08	98.3	95.7	91.2	79.6	63.3	47.4	108.05
94-3	1.30E+08	98.8	97.3	94.9	87	74.3	61	137.29
94-4	1.10E+08	98.5	96.7	93.4	82.5	65.9	50	112.03
60-1	2.60E+09	90.9	85.5	79.3	62.6	40.9	25.8	78.36
60-2	3.10E+09	91.9	87.4	82.6	69.2	49.6	33.7	92.27
60-3	2.70E+09	91.5	86.6	80.9	64.9	43.2	27.7	81.79
60-4	3.40E+09	91.8	87.6	83.3	72.6	55.5	39.6	102.47
60-5	2.70E+09	90.6	85.3	79.2	63.4	42.5	27.4	80.68
10-1	3.10E+09	91.5	86.8	81.9	68.9	49.4	33.4	91.2
10-2	3.20E+09	91.7	87.2	82.7	70.9	52.8	36.7	97
10-3	3.80E+09	92.8	89.1	85.3	75.5	59.7	44.5	113.59
10-4	3.60E+09	92.5	87	81.2	69.4	54.7	41.3	108.23
10-5	3.10E+10	91.4	86.9	82	68.8	49.1	33.2	91.07
89-1	6.00E+09	93.6	90.6	88	83.2	75.9	67.1	177.72
89-2	1.20E+09	82.6	65.5	47	22.3	9.5	4.5	35.36
89-3	2.60E+09	90.2	84.2	77.7	61	39.7	25.1	76.43
89-4	2.60E+09	90.2	84.4	78	61.9	41.1	26.2	78.39
89-5	3.40E+09	91.5	87.1	82.7	71.7	55	39.6	102.88
89-6	4.20E+09	93	89.3	86.1	78.6	66	51.7	126.19

Table S6. Cochran-Armitage trend test on 38 polymorphic SNPs in *RNF213* loci

CHR	SNP	A1	A2	TEST	AFF	UNAFF	CHISQ	DF	P

17	rs7217421	A	G	TREND	248/256	1722/1996	1.478	1	0.2241
17	rs4889968	G	A	TREND	12/484	117/3513	0.8884	1	0.3459
17	rs9916351	C	T	TREND	221/287	1757/1969	2.436	1	0.1186
17	rs12947578	A	G	TREND	202/306	1583/2139	1.444	1	0.2295
17	rs9913317	A	G	TREND	0/502	1/3733	0.1345	1	0.7138
17	rs7219131	C	T	TREND	224/280	1780/1940	2.13	1	0.1444
17	rs12601730	G	T	TREND	12/496	113/3615	0.6745	1	0.4115
17	rs7220465	T	C	TREND	128/374	1092/2636	3.117	1	0.0775
17	rs11869363	C	T	TREND	136/370	1173/2545	4.732	1	0.0296
17	rs12937242	T	C	TREND	77/431	687/3037	3.324	1	0.06827
17	rs8068939	T	G	TREND	125/383	1004/2728	1.193	1	0.2747
17	rs12451223	C	T	TREND	120/388	935/2795	0.501	1	0.4791
17	rs8081176	C	T	TREND	159/349	1265/2467	1.327	1	0.2494
17	rs6565666	A	G	TREND	119/389	649/3085	11.29	1	0.00078
17	rs7225029	A	G	TREND	45/461	280/3450	1.255	1	0.2626
17	rs4889843	G	A	TREND	246/262	1681/2045	1.996	1	0.1577
17	rs9907978	A	G	TREND	146/362	1243/2487	4.172	1	0.0411
17	rs9908583	G	A	TREND	143/359	1232/2456	4.754	1	0.02923
17	rs4890008	T	G	TREND	27/481	151/3577	1.791	1	0.1807
17	rs10782008	G	A	TREND	173/335	1393/2331	2.139	1	0.1436
17	rs8072917	C	T	TREND	173/335	1393/2331	2.148	1	0.1428
17	rs4890009	G	A	TREND	144/358	1242/2484	4.266	1	0.03889
17	rs4890010	C	T	TREND	173/335	1393/2327	2.209	1	0.1372
17	NeuroX_chr17:78319717	T	C	TREND	0/508	2/3732	0.2724	1	0.6018
17	rs11150856	C	T	TREND	68/440	544/3188	0.4948	1	0.4818
17	rs12051723	T	G	TREND	98/410	545/3183	7.603	1	0.005829
17	rs11655038	T	G	TREND	40/468	337/3391	0.7355	1	0.3911
17	rs7216493	G	A	TREND	128/380	1086/2642	3.345	1	0.0674
17	rs8078251	G	A	TREND	170/338	1230/2490	0.03161	1	0.8589
17	rs4078429	G	A	TREND	28/478	198/3532	0.04479	1	0.8324
17	rs6565681	A	G	TREND	76/430	610/3114	0.5957	1	0.4402
17	rs4889848	C	T	TREND	75/433	608/3124	0.7565	1	0.3844
17	rs7224239	G	A	TREND	249/259	1622/2112	5.759	1	0.01641
17	rs12944385	G	A	TREND	3/505	22/3712	1.44E-05	1	0.997
17	rs4890018	C	T	TREND	31/477	210/3516	0.1718	1	0.6785
17	rs8072774	T	C	TREND	40/466	324/3406	0.3454	1	0.5567
17	rs3185057	A	G	TREND	51/457	312/3418	1.541	1	0.2144
17	rs8359	T	C	TREND	42/466	332/3400	0.2201	1	0.6389