Supplemental Tables

Supplemental Table S1. *SCG2* polymorphism location and allele frequencies across populations.

Site #	Alleles[a]	Position[b]	Amino acid	Asian (n=45)	Black (n=55)	Hispanic (n=27)	White (n=53)	Global (n=180)	dbSNP
1	t/C	-725, promoter	none	0	0.01	0	0	0.003	
2	g/A	-453, promoter	none	0	0	0	0.01	0.003	
3	g/T	-253, promoter	none	0.09	0.056	0	0	0.041	
4	t/C	-173, promoter	none	0	0.067	0	0	0.021	
5	T13-16	-157, promoter	none	NA	NA	NA	NA	NA	
6	t/C	-154, promoter	none	0.09	0.067	0	0	0.044	
7	a/G	736, intron 1	none	0.045	0.305	0.04	0.02	0.127	rs1017448
8	t/C	964, intron 1	none	0	0.055	0.04	0.01	0.022	
9	t/C	1098, intron 1	none	0	0.056	0	0	0.017	
10	t/G	1253, intron 1	none	0.142	0.075	0.148	0.048	0.102	rs2894511
11	a/G	1289, intron 1	none	0	0	0.018	0	0.003	
12	g/A	1367, intron 1	none	0.048	0.113	0	0.01	0.046	
13	a/G	1400, intron 1	none	0.024	0.028	0	0.01	0.023	rs16864981
14	a/T	1604, intron 1	none	0	0.01	0	0	0.003	
15	c/T	1624, intron 1	none	0.01	0	0	0	0.003	
16	t/G	1801, intron 1	none	0	0.02	0	0	0.006	
17	g/A	1851, intron 1	none	0	0.036	0	0	0.024	
18	c/T	1995, intron 1	none	0	0	0.01	0.02	0.012	
19	c/T	2327, intron 1	none	0	0.01	0	0	0.003	
20	t/C	2508, intron 1	none	0	0.01	0	0.01	0.006	
21	c/T	2620, intron 1	none	0.01	0	0	0	0.003	rs16864979
22	t/C	2640, intron 1	none	0.01	0	0	0	0.003	
23	g/A	2707, intron 1	none	0	0.036	0	0	0.012	
24	c/A	2843, intron 1	none	0.01	0.036	0	0	0.012	rs16864977
25	t/C	3260, exon 2	Y-61-H	0.01	0	0	0	0.003	rs16864976
26	c/T	3965, exon 2	R-296-W	0	0	0.018	0	0.003	
27	g/A	4066, exon 2	G-329-G	0.01	0	0	0	0.003	
28	t/A	4351, exon 2	T-424-T	0	0.01	0	0	0.003	
29	c/T	4366, exon 2	D-429-D	0	0.155	0.038	0.02	0.058	rs721233
30	a/G	4615, exon 2	L-522-L	0.01	0	0	0.01	0.006	
31	a/G	4698, exon 2	E-540-G	0.01	0	0	0	0.003	
32	c/T	4770, exon 2	P-564-L	0	0	0	0.02	0.006	
33	c/T	4873, exon 2	N-598-N	0	0.028	0	0	0.008	rs16864974
34	t/C	4927, exon 2	N-616-N	0	0.018	0	0	0.006	rs16864973
35	c/A	5024, exon 2 UTR	none	0	0.155	0.038	0.02	0.058	rs2230168
36	t/C	5080, exon 2 UTR	none	0.01	0	0	0	0.003	

[a]Lowercase, major allele; uppercase, minor allele. [b]Relative to putative cap site.

Supplemental Table S2. Comparison of nucleotide sequence diversity ($x10^{-4}$) in SCG2 gene domains across populations.

Sequenced region (bp spanned)	Asian	Black	Hispanic	White	Global
Coding (1851 bp)	0.43 [4]	2.02 [4]	0.6 [2]	0.54 (59)	1.03 [10]
Promoter (1160 bp)	2.86 [2]	3.27 [4]	0 [0]	0.17 [1]	1.87 [5]
5'-UTR (137 bp)	0 [0]	0 [0]	0 [0]	0 [0]	0 [0]
Intron (2988 bp)	1.85 [8]	4.6 [13]	1.6 [5]	0.84 [7]	2.65 [18]
3'-UTR (423 bp)	0.47 [1]	6.25 [1]	1.76 [1]	0.94 [1]	2.73 [2]
Total (6559 bp)	1.5 [15]	3.65 [22]	1.0 [8]	0.63 [12]	2.01 [35]

[ ], Number of SNPs in that region for that population.

Supplemental Table S3. Admixture analysis in black hypertension cases versus controls (UCSD study).

Gene (description)	Chi-sq	DF	Minor allele frequency	Chromosome
ADRB2 (252 G/A rs1042717)	0.11	1	0.27	5
FMO2 (stop)	0.21	1	0.13	1
CACNA1S (intron 1 rs1325309)	1.61	1	0.49	1
NOS3 (298 Glu/Asp rs1799983)	0.78	1	0.11	7
ACE (intron 17 rs4344)	0.34	1	0.39	17
ADD1 (1797 T/C rs4984)	0.01	1	0.21	4
AGTR1/CPB1 (3'-UTR rs5186)	0.22	1	0.10	3
DRD1 (-94 A/G rs5326)	2.57	1	0.21	5
CHGA (3' 12602 C/G rs875395)	0.03	1	0.32	14
ADRA2B (394 Gly/Gly)	0.15	1	0.25	2
ADRB3 (64 Trp/Arg rs4994)	1.10	1	0.11	8
PNMT (1509 G/A)	0.29	1	0.29	17
PYY (3'-UTR 2123 C/A)	0.33	1	0.11	17
CHRNA3 (intron 3)	0.06	1	0.42	15
ADRA1A (rs1048101)	0.10	1	0.28	8
SLC18A1 (rs1497020)	0.79	1	0.05	8
MAOB (rs1799836)	4.09	1	0.23	X
CYB561 (rs2058203)	0.47	1	0.38	17
SLC18A2 (rs363227)	2.57	1	0.33	10
KLK1 (rs5517)	0.84	1	0.19	19
SLC6A5 (NET1 rs5569)	0.17	1	0.17	11
MAOA (rs6323)	0.01	1	0.14	X
TH (81 Val/Met rs6356)	0.25	1	0.13	11
ADRA1C (347 Arg/Cys)	0.00	1	0.29	8
CHRNA5 (rs871058)	0.68	1	0.07	15
GPRK4 (142 Ala/Val)	0.00	1	0.38	4
RGSPX1.3.HF1.1_2	2.74	1	0.18	16
SLC9A3 (rs2247114)	3.35	1	0.16	5
SLC9A3R1 (rs7420)	0.71	1	0.47	17
HSD11B2 (156 Thr/Thr rs5479)	1.40	1	0.17	16
NR3C2 (rs5529)	0.21	1	0.21	4
REN (rs5705)	1.02	1	0.33	1
AGT (rs7079)	0.62	1	0.09	1
	Sum of chi-sqs	Sum of DF	P value	
	27.83	33	0.7233	

Supplemental Table S4. Divergent SCG2 A736G genotype distribution between all unrelated male and female subjects, by chi-square.

Genotype	Male (n=1388)	Female (n=1254)	Chi-square p-value
AA	73 (5.3)	40 (3.2)	P<0.0001
GA	360 (25.9)	255 (20.3)	
GG	955 (68.8)	959 (76.5)	
Genotype	Male (n=1388)	Female (n=1254)	Chi-square p-value
AA+GA	433 (31.2)	295 (23.5)	P<0.0001
GG	955 (68.8)	959 (76.5)	

Supplemental Table S5. SOLAR analysis of the effect of SCG2 G736A on heritability of cardiovascular traits in the GenNet subjects, stratified by gender.

GenNet variable	SCG2 SNP only	Adjusted for age	Females only SCG2 SNP only (n=476)	Males only SCG2 SNP only (n=305)	Females only SCG2 SNP & adjusted for age (n=476)	Males only SCG2 SNP & adjusted for age (n=305)
SBP	0.3996	0.8694	**0.0447**	0.1833	0.1703	0.1269
DBP	0.1930	0.3392	0.0653	0.8819	0.1535	0.7724
PP	0.9239	0.5459	0.2492	**0.0297**	0.5360	**0.0207**
SBP raw	0.1850	0.4965	**0.0135**	0.2150	0.0659	0.1754
SBP med	0.1677	0.5412	**0.0137**	0.2700	0.0770	0.2143
DBP raw	0.1163	0.2013	0.0792	0.6746	0.1556	0.7516
DBP med	0.1026	0.2131	0.0636	0.6787	0.1573	0.7667
PP raw	0.8831	0.6242	0.0819	**0.0302**	0.2745	**0.0208**
PP med	0.7771	0.6553	0.0659	**0.0393**	0.2599	**0.0260**

Key: SBP=systolic blood pressure; DBP=diastolic blood pressure; PP=pulse pressure;
SBP/DBP/PP raw=without taking into account medication; SBP/DBP/PP med=correcting for medication.

Supplemental Table S6. Logistic regression-based gender-specific analysis of the data from all unrelated individuals in five subject cohorts.

Genotype	Males (n=1385) OR (95% CI)	Overall p-value	Females (n=1253) OR (95% CI)	Overall p-value
AA	0.63 (0.37, 1.08)	0.20	1.49 (0.71, 3.10)	**0.019**
GA	1.02 (0.76, 1.36)		1.61 (1.15, 2.26)	
GG	1.00		1.00	
AA+GA	0.95 (0.72, 1.25)	0.69	1.60 (1.15, 2.22)	**0.0050**
GG	1.00		1.00	

Key: OR=odds ratio. Note that the genotype effects were adjusted for study and age by treating these factors as covariates in the regression analysis.

Supplemental Table S7. Neutrality tests for polymorphism at SCG2.

Population	Tajima's D	Fu's *Fs*	Fu and Li's D*	Fu and Li's F*	Fu and Li's D	Fu and Li's F	Fay and Wu's H
Asian (n=90)	-1.487	-6.883**	-1.40986	-1.70977	-1.45816	-1.75506	-3.259*
Black (n=110)	-0.869	-4.833**	-0.062	-0.428	-0.076	-0.446	-3.118*
Hispanic (n=54)	-1.101	-1.078	-0.11777	-0.49715	-0.14006	-0.5204	-3.385*
White (n=106)	-1.836*	-5.962**	-2.7519	-2.88875	-0.8455	-1.3955	-5.712**
Global (n=360)	-1.52	-14.485**	-1.42719	-1.78364	-1.44598	-1.79994	-4.637**

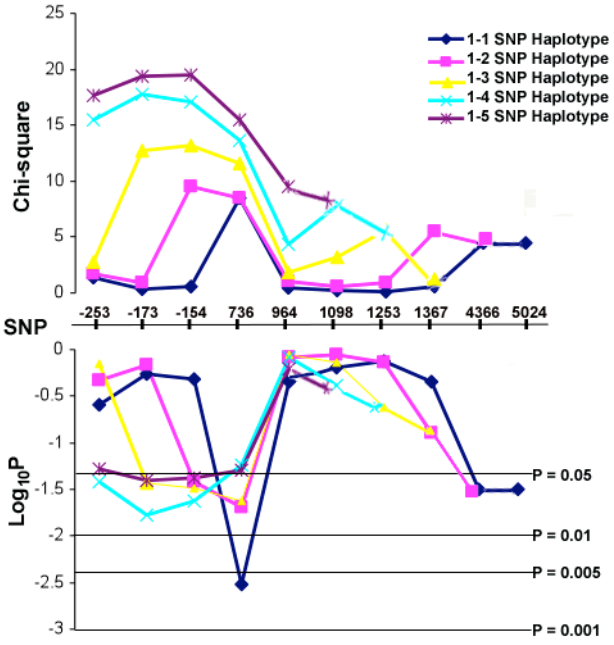
*:P<0.05. **: P<0.01.

Supplemental Table S8. SCG2 haplotype distributions across populations.

Haplotype no.	Haplotype	Asian (n=90)	Black (n=110)	Hispanic (n=54)	White (n=106)	Global (n=360)
1	GCTTG	0.811 (73)	0.573 (63)	0.833 (45)	0.934 (99)	0.778 (280)
2	GCTGG	0.133 (12)	0.073 (8)	0.148 (8)	0.047 (5)	0.092 (33)
3	ACTTG	0.011 (1)	0.191 (21)	0 (0)	0 (0)	0.061 (22)
4	ACTTA	0.033 (3)	0.055 (6)	0 (0)	0.009 (1)	0.028 (10)
5	ATTTG	0 (0)	0.055 (6)	0.019 (1)	0.009 (1)	0.022 (8)
6	ACCTA	0 (0)	0.055 (6)	0 (0)	0 (0)	0.017 (6)
7	GCTTA	0.011 (1)	0 (0)	0 (0)	0 (0)	0.003 (1)

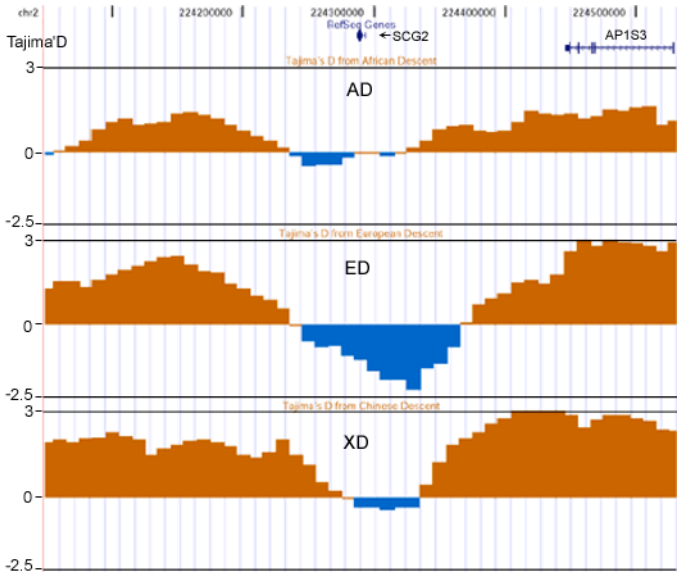
Supplemental Figures and Figure Legends.

Supplemental Figure S1



Supplemental Figure S1. Sliding window analysis for haplotype association in African Americans. Haplotypes were constructed with 1 to 5 consecutive variant sites from nine SNPs common in African Americans (number for each SNP denotes position; see Supplemental Table S1). Case-control haplotype association to hypertension was analyzed by program SNPEM (http://polymorphism.ucsd.edu/cgi-bin/PRL/snpem/snpem.cgi) software as described (61). Upper panel shows chi-square value, low panel is converted P value with significant P values indicated.

Supplemental Figure S2



Supplemental Figure S2. Tajima's D in sliding window format is shown across 481,860 bp of chromosome 2 centered on *SCG2* from three human populations. Orange color represents positive Tajima's D (maximum is 3), while blue represents negative value (minimum is –2.5). AD: African Descent; ED: European Descent; XD: Chinese Descent.