

Table S3 Continued

Gene	SNP (position)	Genotype	Screening Panel			Odds ratio (p-value)			
			Genotype frequency	HWE	Call rate	Allelic	Recessive	Dominant	Additive
DLGAP2	rs2301963	CC/CA/AA	510	0.024	98.6	1.05	1.07	1.08	(0.516)
		NT	497	0.029		(0.239)	(0.368)	(0.321)	
BRCC1	rs2298881	CC/CA/AA	595	0.161	97.5	1.00	0.96	1.04	(0.702)
		NT	600	0.821		(0.948)	(0.642)	(0.616)	
FOXO3	rs7158	AA/AG/GG	511	0.327	97.9	1.01	1.09	0.95	(0.262)
		NT	545	0.187		(0.850)	(0.264)	(0.452)	
GDF2	rs3747676	GG/GA/AA	415	0.839	96.4	1.01	1.07	0.94	(0.309)
		NT	444	0.050		(0.892)	(0.340)	(0.424)	
GIPC1	rs3815715	GG/GA/AA	734	0.040	98.8	1.03	0.98	1.07	(0.510)
		NT	728	0.532		(0.585)	(0.794)	(0.330)	
GNA14	rs1801258	TT/TC/CC	317	0.888	99.0	1.05	1.11	0.90	(0.249)
		NT	330	0.039		(0.321)	(0.128)	(0.903)	
GNAI2	rs2236943	GG/GA/AA	556	0.137	97.9	1.04	1.02	1.07	(0.640)
		NT	543	0.448		(0.427)	(0.751)	(0.345)	
GUCA1C	rs2715709	AA/GA/GG	225	0.204	97.1	1.06	1.12	0.98	(0.156)
		NT	236	0.373		(0.242)	(0.081)	(0.824)	
HCN4	rs3743496	GG/TG/TT	431	0.002	98.2	1.01	0.94	1.11	(0.150)
		NT	408	0.710		(0.859)	(0.369)	(0.192)	
HLA-DMB	rs2071556	CC/CA/AA	511	0.534	98.0	1.09	1.17	1.07	(0.105)
		NT	500	0.036		(0.060)	(0.035)	(0.346)	
KCNP2	rs755381	TT/TC/CC	453	0.044	98.2	1.05	1.03	1.12	(0.311)
		NT	425	0.548		(0.245)	(0.688)	(0.128)	

Table S3 Continued

Gene	SNP (position)	Genotype	Screening Panel			Odds ratio (p-value)			
			Genotype frequency	HWE	Call rate	Allelic	Recessive	Dominant	Additive
KCNMB4	rs710652	CC/AC/AA	660	0.131	99.2	1.09	1.28	1.03	(0.012)
		NT	953	0.083		(0.056)	(0.003)	(0.638)	
KCNN1	rs2278993	TT/TC/CC	189	0.513	99.2	1.07	1.08	1.15	(0.335)
		NT	805	0.924		(0.152)	(0.259)	(0.207)	
PPP1R1B	rs3764352	TT/TC/CC	547	0.412	96.0	1.07	1.16	1.04	(0.165)
		NT	940	0.333		(0.156)	(0.059)	(0.621)	
PTHR1	rs1138518	TT/TC/CC	381	0.626	98.5	1.01	1.04	0.98	(0.803)
		NT	931	0.169		(0.814)	(0.599)	(0.843)	
PTPRT	rs3746539	AA/AG/GG	495	0.119	99.1	1.04	1.12	0.99	(0.262)
		NT	991	0.644		(0.435)	(0.139)	(0.863)	
RAC2	rs929023	TT/TC/CC	387	0.448	98.2	1.06	1.06	1.12	(0.373)
		NT	921	0.951		(0.200)	(0.438)	(0.173)	
RGS2	rs3767489	AA/GA/GG	635	0.075	98.0	1.03	0.94	1.12	(0.104)
		NT	961	0.291		(0.483)	(0.476)	(0.099)	
RGS20	rs3816772	CC/CG/GG	268	0.162	97.6	1.03	1.11	0.92	(0.112)
		NT	981	0.152		(0.543)	(0.132)	(0.377)	
SLC13A1	rs2140516	GG/GA/AA	341	0.448	99.4	1.06	1.11	1.03	(0.322)
		NT	917	0.039		(0.225)	(0.135)	(0.736)	
SLC22A7	rs2270860	AA/GA/GG	233	0.800	97.8	1.1	1.15	1.09	(0.100)
		NT	868	0.352		(0.048)	(0.032)	(0.406)	
SLC26A8	rs2295852	TT/TC/CC	994	0.413	97.6	1.01	0.97	1.03	(0.857)
		NT	747	0.926		(0.835)	(0.806)	(0.690)	

Table S3 Continued

Gene	SNP (position)	Genotype	Screening Panel				Odds ratio (p-value)			
			Genotype frequency	HWE	Call rate	Allelic	Recessive	Dominant	Additive	
SLC2A11	rs2236620	AA/AG/GG	308	0.266	99.0	1.04	1.00	1.16	(0.211)	
		HT	715	0.306		(0.360)	(0.956)	(0.092)		
SLCO1B1	rs2291075	GG/GA/AA	279	0.039	98.7	1.01	0.95	1.05	(0.493)	
		HT	719	0.680		(0.866)	(0.524)	(0.466)		
WNK1	rs2255390	GG/GA/AA	490	0.359	97.4	1.07	1.09	1.10	(0.339)	
		HT	516	0.470		(0.139)	(0.262)	(0.201)		

The replication panel consists of 1,929 hypertensive cases and 1,993 normotensives controls selected from a 11,569 cohort sample (Table S2).

Table S4 Clinical characteristics of the screening panel

Parameters	Hypertensive cases (758)	Normotensive controls (726)
Male (n (%))	564 (74.4)	550 (75.8)
Age (years)	59.0±11.0	62.8±9.4
Body mass index (kg/m ²)	23.6±3.0	22.7±2.9
Systolic BP (mmHg)	163.5±24.6	115.9±12.0
Diastolic BP (mmHg)	100.3±15.7	72.0±7.6
Antihypertensive medication (n (%))	499 (65.8)	-

Values are mean±standard deviation. Hypertensive cases: non-obese hypertensive patients, who had a previous diagnosis of hypertension at between 30 and 59 years of age, were either being treated with antihypertensive medication or had a SBP more than 160 mmHg and/or DBP more than 100 mmHg, had a family history of hypertension in their parents and/or siblings. Normotensive controls: middle-aged to elderly subjects (aged more than 45 years), who had never been treated with antihypertensive medications, had a SBP less than 120 mmHg and DBP less than 80 mmHg, and had no family history of hypertension.

Table S5 Dense SNP analysis of the *ATP2B1* gene (screening panel)

Gene	SNP (position)	Genotype	Screening Panel				Odds ratio (p-value)			
			Genotype frequency	HWE	Call rate	Allelic	Recessive	Dominant	Additive	
ATP2B1	rs3920010 (88464519)	GG/GA/AA	17	0.971	97.9	0.95	0.72	0.97	(0.596)	
		HT	191	0.187		(0.591)	(0.311)	(0.808)		
	rs3900133 (88512561)	CC/CA/AA			NF					
		HT								
	rs1401982 (88513730)	AA/AG/GG	318	0.603	96.3	1.28	1.34	1.45	(0.006)	
		HT	328	0.474		(0.001)	(0.007)	(0.014)		
	rs988111 (88515650)	TT/TC/CC	249		NF					
		HT	324							
	rs10858912 (88515998)	GG/GA/AA			NF					
		HT								
	rs4516026 (88518251)	TT/TG/GG			NF					
		HT								
	rs2854371 (88519597)	GG/GA/AA	23	0.692	98.7	1.32	1.38	1.37	(0.028)	
		HT	208	0.300		(0.008)	(0.333)	(0.008)		
	rs1520184 (88520698)	GG/GA/AA	16		NF					
		HT	159							
rs1356819 (88524892)	AA/AC/CC	743	0.927	98.6	1.26	1.26	0.90	(0.389)		
	HT	5	0.910		(0.707)	(0.706)	(0.599)			
rs957525 (88524946)	TT/TC/CC	414	0.034	97.6	1.05	1.11	0.90	(0.389)		
	HT	264	0.753		(0.554)	(0.303)	(0.599)			
rs17017109 (88528238)	TT/TG/GG	591	0.586	97.8	0.81	0.79	0.89	(0.211)		
	HT	144	0.816		(0.094)	(0.079)	(0.842)			

Table S5 Continued

Gene	SNP (position)	Genotype	Screening Panel				Odds ratio (p-value)					
			Genotype frequency	HWE	Call rate	Allelic	Recessive	Dominant	Additive			
ATP2B1	rs12579302 (88574634)	GG/GA/AA	HT	105	310	333	0.018	98.9	0.80 (0.004)	0.76 (0.058)	0.76 (0.011)	0.76 (0.023)
		NT	127	319	273	0.046						
	rs11105359 (88575212)	TT/TG/GG	HT					NF				
		NT										
	rs11105360 (88575303)	TT/TC/CC	HT					NF				
		NT										
	rs11105361 (88576810)	CC/CA/AA	HT					NF				
		NT										
	rs7131965 (88590466)	TT/TC/CC	HT	731	15	0	0.025	98.7	0.90 (0.778)	0.83 (0.627)		0.83 (0.468)
		NT	707	11	1	0.990						
	rs11105364 (88593407)	TT/TG/GG	HT	335	322	88	0.276	97.2	1.29 (0.001)	1.36 (0.004)	1.44 (0.016)	1.36 (0.005)
		NT	261	323	113	0.295						
	rs11105368 (88598572)	GG/GC/CC	HT	349	284	89	0.883	94.0	1.25 (0.005)	1.21 (0.082)	1.53 (0.005)	1.21 (0.015)
		NT	294	260	119	0.212						
	rs7136259 (88605319)	TT/TC/CC	HT	323	325	87	0.348	97.2	1.24 (0.006)	1.22 (0.063)	1.50 (0.007)	1.22 (0.016)
		NT	277	312	119	0.389						
rs17836871 (88606297)	TT/TC/CC	HT	419	260	61	0.025	97.8	1.08 (0.368)	1.16 (0.153)	0.90 (0.577)	1.16 (0.202)	
	NT	376	282	53	0.990							
rs11105378 (88614872)	TT/TC/CC	HT	76	301	359	0.276	97.3	0.73 (6.3*10 ⁻⁵)	0.64 (0.005)	0.69 (4.2*10 ⁻⁴)	0.64 (4.6*10 ⁻⁴)	
	NT	108	320	280	0.295							
rs12230074 (88614998)	GG/GA/AA	HT	83	328	332	0.883	97.6	0.82 (0.013)	0.70 (0.021)	0.82 (0.068)	0.70 (0.036)	
	NT	108	316	282	0.212							

Table S5 Continued

Gene	SNP (position)	Genotype	Screening Panel			Odds ratio (p-value)			
			Genotype frequency	HWE	Call rate	Allelic	Recessive	Dominant	Additive
ATP2B1	rs11105379 (88619304)	TT/TC/CC	450	0.348	96.3	1.11 (0.261)	1.12 (0.292)	1.16 (0.520)	(0.542)
		NT	240	0.389					
	rs10858918 (88620476)	HT	40	0.998	98.6	0.90 (0.212)	0.82 (0.378)	0.89 (0.267)	(0.456)
		NT	266	0.852					
	rs2113894 (88623528)	AA/AT/TT	459	0.063	96.3	1.12 (0.200)	1.14 (0.228)	1.17 (0.482)	(0.458)
		NT	232	0.090					
	rs1358350 (88626023)	HT	49	<0.001	91.8	0.85 (0.085)	0.82 (0.345)	0.84 (0.113)	(0.263)
		NT	202	<0.001					
	rs12369944 (88626925)	CC/CA/AA	617	<0.001	94.5	1.27 (0.066)	1.33 (0.043)	1.01 (0.976)	(0.104)
		NT	97	0.013					
	rs2280715 (88627833)	HT	463	<0.001	97.0	1.14 (0.137)	1.16 (0.166)	1.17 (0.425)	(0.364)
		NT	223	0.001					
	rs11105381 (88630966)	GG/GA/AA	452	0.990	98.2	1.09 (0.334)	1.09 (0.398)	1.18 (0.479)	(0.621)
		NT	259	0.843					
	rs1590008 (88631856)	HT	438	0.818	98.2	1.11 (0.243)	1.12 (0.288)	1.18 (0.443)	(0.508)
		NT	265	0.767					

The screening panel is comprised of 758 middle age-onset severe hypertensive patients and 726 middle-aged to elderly evidently normotensive controls (Table S4). NF; no genotype frequency

Table S6 Association of 17 ATP2B4 SNPs with hypertension (screening panel)

Gene	SNP (position)	Genotype	Screening Panel				Odds ratio (p-value)						
			Genotype frequency	HWE	Call rate	Allelic	Recessive	Dominant	Additive				
ATP2B4	rs4245719	GG/GA/AA	HT	287	343	117	0.389	98.5	0.90 (0.153)	0.90 (0.307)	0.82 (0.175)	0.90 (0.332)	
		NT		293	327	94	0.854						
	rs4600103	GG/GA/AA	HT	286	312	129	0.007	94.3	1.03 (0.678)	1.08 (0.466)	0.98 (0.860)		0.98 (0.685)
		NT		252	304	117	0.128						
	rs17537593	TT/TA/AA	HT	64	237	432	<0.001	96.6	1.03 (0.704)	1.33 (0.154)	0.97 (0.761)		1.33 (0.252)
		NT		47	246	407	0.240						
	rs4951273	GG/GC/CC	HT	114	339	289	0.377	97.9	1.11 (0.178)	1.21 (0.214)	1.11 (0.323)		1.11 (0.383)
		NT		93	323	295	0.756						
	rs12749310	GG/GA/AA	HT	427	245	56	0.014	96.1	1.03 (0.766)	1.10 (0.370)	0.81 (0.305)		1.10 (0.256)
		NT		393	261	44	0.940						
	rs4297354	GG/GA/AA	HT	462	227	40	0.087	96.1	1.20 (0.047)	1.27 (0.028)	1.11 (0.662)		1.11 (0.086)
		NT		402	253	42	0.794						
	rs11576343	TT/TC/CC	HT	53	251	432	0.051	97.3	0.92 (0.323)	1.02 (0.918)	0.87 (0.202)		1.02 (0.382)
		NT		50	266	392	0.597						
rs6594013	TT/TA/AA	HT	163	348	231	0.141	97.9	0.95 (0.443)	0.98 (0.856)	0.89 (0.310)		0.98 (0.587)	
	NT		159	348	204	0.647							
rs16852152	GG/GA/AA	HT	437	252	38	0.831	95.9	0.92 (0.354)	0.92 (0.449)	0.82 (0.418)		0.92 (0.618)	
	NT		432	234	30	0.812							
rs3766752	GG/GA/AA	HT	210	367	167	0.782	97.8	1.09 (0.225)	1.15 (0.235)	1.10 (0.433)		1.10 (0.454)	
	NT		180	356	171	0.847							
rs11808688	GG/GA/AA	HT	197	372	169	0.795	96.9	0.94 (0.389)	0.86 (0.183)	1.00 (0.985)		0.86 (0.370)	
	NT		209	331	160	0.189							

Table S6 Continued

Gene	SNP (position)	Genotype	Screening Panel				Odds ratio (p-value)		
			Genotype frequency	HWE	Call rate	Allelic	Recessive	Dominant	Additive
ATP2B4	rs4951130	GG/GA/AA	410	0.758	97.2	1.21	1.22	1.40	(0.082)
		HT	278	0.421		(0.025)	(0.058)	(0.086)	
	rs12095268	TT/TA/AA	367	0.982	98.0	1.09	1.09	1.19	(0.556)
		HT	313	0.599		(0.303)	(0.439)	(0.335)	
	rs12410036	TT/TC/CC	48	0.200	97.7	0.90	0.93	0.87	(0.434)
		HT	256	0.599		(0.232)	(0.720)	(0.196)	
	rs7547344	GG/GA/AA	172	0.618	97.7	1.00	1.02	0.98	(0.954)
		HT	362	0.951		(0.977)	(0.875)	(0.846)	
	rs955865	GG/GA/AA	208	0.677	98.6	0.95	0.96	0.89	(0.668)
		HT	368	0.765		(0.456)	(0.733)	(0.370)	
	rs955866	TT/TC/CC	170	0.712	98.5	1.05	1.11	1.04	(0.702)
		HT	366	0.758		(0.489)	(0.401)	(0.756)	

The screening panel is comprised of 758 middle age-onset severe hypertensive patients and 726 middle-aged to elderly evidently normotensive controls (Table S4).

Table S7 Meta-analysis of ATP2B1 SNPs with hypertension

SNP	Coded Allele	Millennium GPJ			Global BPgen			Pooled		
		OR (95% CI)	P	N	OR (95% CI)	P	N	OR (95% CI)	P	N
rs1401982	A	1.19 (1.11-1.29)	1.3*10 ⁻⁶	9,967	1.07 (1.02-1.12)	0.010	19126	1.10 (1.06-1.15)	1.5*10 ⁻⁶	29,093
rs2681472	A	1.21 (1.13-1.30)	1.8*10 ⁻⁷	10,039	1.14 (1.06-1.22)	2.2*10 ⁻⁴	19055	1.17 (1.12-1.23)	2.1*10 ⁻¹⁰	29,094
rs11105364	T	1.21 (1.13-1.30)	1.5*10 ⁻⁷	10,014	1.13 (1.06-1.21)	4.6*10 ⁻⁴	19151	1.17 (1.11-1.22)	3.1*10 ⁻¹⁰	29,165
rs11105378	C	1.21 (1.13-1.30)	1.5*10 ⁻⁷	9,972	1.13 (1.05-1.21)	5.9*10 ⁻⁴	18894	1.17 (1.11-1.23)	7.0*10 ⁻¹⁰	28,866

In both Japanese Millennium GPJ and Global BP gen, hypertensive subjects were defined as being treated with antihypertensive medication, or SBP greater or equal to 140 mmHg, or DBP greater or equal to 90 mmHg; normotensive subjects were defined as all of not treated with antihypertensive medication, and SBP less or equal to 120 mmHg, and DBP less or equal to 85 mmHg [8]. Adjusted odds ratio was calculated under additive model using multiple logistic regression analysis adjusted for age, age², sex, BMI, and cohort variables. Within Global BPgen, individual cohort results were combined using inverse variance weighted meta-analysis of the effects on a log-odds-ratio scale.

Table S8 Association of ATP2B1 SNPs and blood pressure traits in each Japanese cohort

SNP	coded allele		cohort						SBP			DBP		
	allele	%	name	n	HWE	CR	coefficient	SE	p	coefficient	SE	p		
rs1401982		61.9	Ohasama	1569	0.227	98.6	0.35	0.60	0.558	0.06	0.39	0.868		
		62.3	Yokohama	2269	0.588	99.1	-1.51	0.43	4.2*10⁻⁴	-0.75	0.29	0.009		
		62.6	Shigaraki	2191	0.908	96.4	-1.72	0.56	0.002	-0.91	0.35	0.010		
	A	61.8	Takashima	1718	0.302	99.3	-1.95	0.72	0.007	-0.90	0.41	0.028		
		61.7	Suita	2529	0.506	99.7	-0.80	0.57	0.160	-0.44	0.33	0.182		
		62.0	Matsuyama	803	0.175	99.4	-1.27	0.97	0.194	-1.39	0.62	0.026		
		63.8	Nomura	2865	0.611	99.6	-1.39	0.56	0.020	-0.67	0.33	0.045		
		62.1	Ohasama	1587	0.226	99.7	0.38	0.60	0.522	0.06	0.39	0.887		
		62.6	Yokohama	2278	0.321	99.5	-1.52	0.43	3.8*10⁻⁴	-0.78	0.28	0.006		
rs2681472		63.5	Shigaraki	2254	0.701	99.2	-2.03	0.56	2.9*10⁻⁴	-1.15	0.35	0.001		
	A	62.3	Takashima	1718	0.257	99.3	-2.25	0.72	0.002	-1.03	0.41	0.013		
		62.1	Suita	2528	0.655	99.7	-0.97	0.57	0.089	-0.49	0.33	0.131		
		62.1	Matsuyama	802	0.191	99.3	-1.13	0.98	0.248	-1.39	0.62	0.026		
		64.3	Nomura	2865	0.907	99.6	-1.42	0.60	0.018	-0.69	0.34	0.041		
		62.2	Ohasama	1589	0.203	99.8	0.42	0.60	0.477	0.12	0.39	0.766		
		63.3	Yokohama	2277	0.414	99.4	-1.61	0.43	1.8*10⁻⁴	-0.79	0.29	0.006		
		64.3	Shigaraki	2234	0.410	98.3	-2.11	0.56	1.7*10⁻⁴	-1.16	0.35	0.001		
	T	62.7	Takashima	1727	0.570	99.8	-2.25	0.71	0.002	-0.98	0.41	0.017		
rs11105364		62.4	Suita	2530	0.635	99.8	-1.08	0.57	0.058	-0.54	0.33	0.096		
		62.8	Matsuyama	805	0.285	99.6	-1.05	0.98	0.285	-1.35	0.62	0.031		
		64.4	Nomura	2851	0.495	99.1	-1.30	0.60	0.030	-0.60	0.34	0.077		

Table S8 Continued

SNP	coded allele		cohort				SBP			DBP		
	allele	%	name	n	HWE	CR	coefficient	SE	p	coefficient	SE	p
rs11105378	C	62.9	Ohasama	1566	0.478	98.4	0.31	0.60	0.600	-0.04	0.39	0.914
		63.4	Yokohama	2258	0.244	98.6	-1.32	0.43	0.002	-0.66	0.29	0.022
		65.2	Shigaraki	2213	0.141	97.4	-2.45	0.56	1.3*10⁻⁵	-1.31	0.35	2.2*10⁻⁴
		63.2	Takashima	1722	0.237	99.5	-2.41	0.72	8.5*10⁻⁴	-1.15	0.41	0.006
		63.0	Suita	2521	0.498	99.4	-1.00	0.58	0.084	-0.42	0.33	0.207
	63.2	Matsuyama	803	0.434	99.4	-1.14	0.99	0.249	-1.56	0.63	0.014	
	65.7	Nomura	2865	0.468	99.6	-1.11	0.60	0.065	-0.47	0.34	0.164	

Coefficients and standardized error for systolic and diastolic BP were calculated under additive model using multiple regression analysis adjusted for age, age², sex, BMI. Adjustment for treatment with antihypertensive medication was achieved by adding fixed constants to measured values (+15mmHg for SBP and -10mmHg for DBP). CR indicates call rate.

Table S9 Association of European GWAS-derived SNPs with hypertension in the Japanese screening and replication panels

SNP	Genotype	Screening panel					Replication panel					overall Odds (p value)
		HT	NT	Genotype frequency	HWE	Call rate	Odds (p value)	Genotype frequency	HWE	Call rate	Odds (p value)	
rs1458038	TT/TC/CC	92	81	338	315	0.928	98.0	1.19	0.047	97.9	1.21	1.20 (9.9*10 ⁻⁶)
rs1004467	AA/AG/GG	380	299	66	0.514	98.6	1.35 (1.4*10 ⁻⁴)	0.034	99.8	1.09 (0.079)	1.16 (4.9*10 ⁻⁴)	
rs1378942	CC/CA/AA	483	236	25	0.557	98.0	1.09	0.853	98.9	1.04 (0.536)	1.05 (0.305)	
rs12946454	TT/TA/AA	28	13	207	499	0.107	0.256	0.140	99.7	0.99 (0.907)	1.03 (0.624)	
rs381815	TT/TC/CC	27	31	242	483	0.624	98.8	1.05	0.033	99.4	0.99 (0.913)	1.01 (0.852)
rs6495122	AA/AC/CC	508	204	21	0.924	96.8	1.18	0.263	99.2	1.10 (0.102)	1.12 (0.021)	
rs9815354	AA/AG/GG	7	142	598	0.654	98.5	0.90	0.265	98.9	1.05 (0.463)	1.01 (0.873)	

The screening panel is comprised of 758 middle age-onset severe hypertensive patients and 726 middle-aged to elderly evidently normotensive controls (Table S4). The replication panel consists of 1,929 hypertensive cases and 1,993 normotensives controls selected from a 11,569 cohort sample were enrolled (Table S2). Odds ratios and p-values for allelic model are shown.

Table S10 Association of European GWAS-derived SNPs and blood pressure traits in each Japanese cohort

SNP	coded allele		cohort					SBP			DBP		
	allele	%	name	n	HWE	CR	coefficient	SE	p	coefficient	SE	p	
EGFS rs1458038		33.7	Ohasama	1557	0.174	97.8	1.58	0.60	0.008	0.44	0.39	0.260	
		33.5	Yokohama	2223	0.005	97.1	0.84	0.44	0.055	0.46	0.29	0.115	
		33.8	Shigaraki	2156	0.001	94.9	1.17	0.56	0.037	0.46	0.35	0.196	
	T	31.4	Takashima	1714	0.163	99.1	2.43	0.73	0.001	1.62	0.42	1.0*10⁻⁴	
		33.6	Suita	2533	0.508	99.9	0.67	0.58	0.250	0.43	0.33	0.191	
		33.4	Matsuyama	804	0.459	99.5	0.70	1.04	0.500	0.54	0.67	0.414	
	38.2	Nomura	2841	0.105	98.8	1.85	0.58	0.002	1.09	0.33	0.001		
GYP17A1 rs1004467		70.2	Ohasama	1579	0.254	99.2	1.41	0.45	0.002	0.48	0.30	0.110	
		68.4	Yokohama	2276	0.812	99.4	1.05	0.57	0.065	0.03	0.36	0.938	
		65.5	Shigaraki	2244	0.898	98.7	1.46	0.74	0.050	0.83	0.43	0.051	
	A	67.8	Takashima	1714	0.573	99.1	-0.21	0.59	0.721	-0.34	0.34	0.308	
		66.8	Suita	2533	0.865	99.9	0.12	1.05	0.911	-0.10	0.67	0.885	
		67.4	Matsuyama	804	0.388	99.5	1.25	0.62	0.045	0.50	0.35	0.149	
	69.7	Nomura	2859	0.475	99.4	1.41	0.45	0.002	0.48	0.30	0.110		
CSK rs1378942		77.7	Ohasama	1575	0.821	98.9	-0.17	0.68	0.804	-0.53	0.45	0.241	
		78.1	Yokohama	2245	0.152	98.0	0.73	0.52	0.157	0.48	0.35	0.167	
		83.0	Shigaraki	2225	0.187	97.9	1.80	0.71	0.012	1.35	0.45	0.003	
	C	80.7	Takashima	1703	0.808	98.4	-0.41	0.88	0.644	0.08	0.51	0.870	
		80.5	Suita	2528	0.098	99.7	1.28	0.69	0.063	0.43	0.39	0.270	
		79.7	Matsuyama	798	0.846	98.8	0.24	1.21	0.842	0.07	0.77	0.923	
	81.0	Nomura	2848	0.075	99.0	1.18	0.72	0.103	0.63	0.41	0.121		

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Table S10 Continued

SNP	coded allele		cohort					SBP			DBP		
	allele	%	name	n	HWE	CR	coefficient	SE	p	coefficient	SE	p	
DLCD3 rs12946454		81.6	Ohasama	1583	0.356	99.4	1.76	0.72	0.015	0.99	0.48	0.038	
		83.0	Yokohama	2274	0.517	99.3	0.23	0.56	0.687	0.12	0.37	0.752	
		83.3	Shigaraki	2242	0.966	98.6	0.46	0.72	0.524	0.76	0.46	0.094	
	T	85.3	Takashima	1712	0.707	99.0	-1.37	0.98	0.163	-1.09	0.56	0.052	
		83.2	Suita	2528	0.234	99.7	0.53	0.73	0.464	0.08	0.42	0.845	
		82.4	Matsuyama	805	0.799	99.6	0.34	1.28	0.790	0.86	0.82	0.290	
	82.4	Nomura	2861	0.142	99.5	-0.35	0.75	0.635	-0.05	0.42	0.899		
LEKHA7 rs381815		15.1	Ohasama	1590	0.566	99.9	0.22	0.79	0.778	0.23	0.52	0.657	
		19.7	Yokohama	2281	0.457	99.6	-0.77	0.52	0.139	0.04	0.35	0.900	
		19.3	Shigaraki	2248	0.587	98.9	-0.38	0.68	0.574	-0.90	0.43	0.034	
	T	19.0	Takashima	1719	0.434	99.4	-0.196	0.87	0.271	-0.22	0.50	0.660	
		20.2	Suita	2527	0.421	99.6	0.76	0.69	0.272	0.42	0.40	0.289	
		20.2	Matsuyama	808	0.496	100.0	0.99	1.19	0.408	0.53	0.76	0.489	
	23.2	Nomura	2859	0.007	99.4	0.88	0.66	0.187	0.73	0.37	0.052		
CSK-ULK3 rs6495122		79.4	Ohasama	1581	0.050	99.3	-0.39	0.69	0.569	-0.46	0.45	0.308	
		78.4	Yokohama	2288	0.157	99.9	0.88	0.51	0.086	0.66	0.34	0.055	
		83.5	Shigaraki	2237	0.146	98.4	0.96	0.72	0.183	0.96	0.45	0.034	
	A	80.6	Takashima	1720	0.221	99.4	0.03	0.86	0.969	0.06	0.49	0.907	
		81.6	Suita	2529	0.004	99.7	0.87	0.69	0.211	0.18	0.40	0.654	
		81.5	Matsuyama	806	0.734	99.8	1.35	1.24	0.276	0.68	0.79	0.391	
	82.6	Nomura	2855	0.115	99.3	1.16	0.75	0.120	0.64	0.42	0.129		

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Table S10 Continued

SNP	coded allele		cohort				SBP			DBP		
	allele	%	name	n	HWE	CR	coefficient	SE	p	coefficient	SE	p
rs9815354		14.9	Ohasama	1569	0.749	98.6	-0.08	0.80	0.918	0.32	0.53	0.543
		10.5	Yokohama	2269	0.122	99.1	-1.01	0.67	0.134	-0.44	0.45	0.331
		12.7	Shigaraki	2252	0.099	99.1	-1.58	0.80	0.047	-0.10	0.50	0.846
	A	12.0	Takashima	1710	0.201	98.8	-0.57	1.08	0.600	0.15	0.62	0.802
		11.9	Suita	2521	0.456	99.4	-1.03	0.86	0.232	-0.08	0.49	0.867
		11.4	Matsuyama	804	0.389	99.5	-0.91	1.50	0.547	0.70	0.96	0.467
		9.1	Normura	2853	0.632	99.2	0.79	1.00	0.427	1.21	0.56	0.030

Coefficients and standardized error for systolic and diastolic BP were calculated under additive model using multiple regression analysis adjusted for age, age², sex, BMI. Adjustment for treatment with antihypertensive medication was achieved by adding fixed constants to measured values (+15mmHg for SBP and +10mmHg for DBP).

Table S11 Multiple linear regression analysis for BP trait and hypertension

Parameters	Coded allele	Systolic blood pressure		Diastolic blood pressure		Hypertension			
		Coefficient	Standardized coefficient	P	Coefficient	Standardized coefficient	P	Odds (95% C.I.)	P
Sex		2.38	0.05	<0.001	3.15	0.12	<0.001	1.33 (1.18-1.50)	<0.001
Age (years)		0.31	0.19	<0.001	0.96	1.03	<0.001	1.15 (1.12-1.19)	<0.001
Age ²		0.00	0.25	<0.001	-0.01	-0.74	<0.001	0.99 (0.99-0.99)	0.008
Body mass index (kg/m ²)		1.80	0.25	<0.001	1.12	0.27	<0.001	1.28 (1.26-1.30)	<0.001
Habitual drinking		0.79	0.02	0.035	0.93	0.04	<0.001	1.24 (1.11-1.40)	<0.001
ATP2B1 rs11105378	C	1.32	0.04	4.4*10 ⁻⁸	0.71	0.04	6.1*10 ⁻⁷	1.21 (1.12-1.30)	4.0*10 ⁻⁷
EGF5 rs1458038	T	1.36	0.04	1.5*10 ⁻⁸	0.77	0.04	6.4*10 ⁻⁸	1.20 (1.11-1.29)	1.4*10 ⁻⁶
CYP17A1 rs1004467	A	0.97	0.03	8.9*10 ⁻⁵	0.35	0.02	0.017	1.14 (1.06-1.23)	8.4*10 ⁻⁴
CSK rs1378942	C	0.71	0.02	0.014	0.36	0.02	0.036	1.09 (1.00-1.19)	0.046

Coefficients for systolic and diastolic BP were calculated using multiple linear regression analysis adjusted cohort variables. Adjustment for treatment with antihypertensive medication was achieved by adding fixed constants to measured values (+15mmHg for SBP and +10mmHg for DBP). Hypertensive subjects were defined as being treated with antihypertensive medication, or SBP greater or equal to 140 mmHg, or DBP greater or equal to 90 mmHg; normotensive subjects were defined as all of not treated with antihypertensive medication, and SBP less or equal to 120 mmHg, and DBP less or equal to 85 mmHg [8].

FIGURE S1

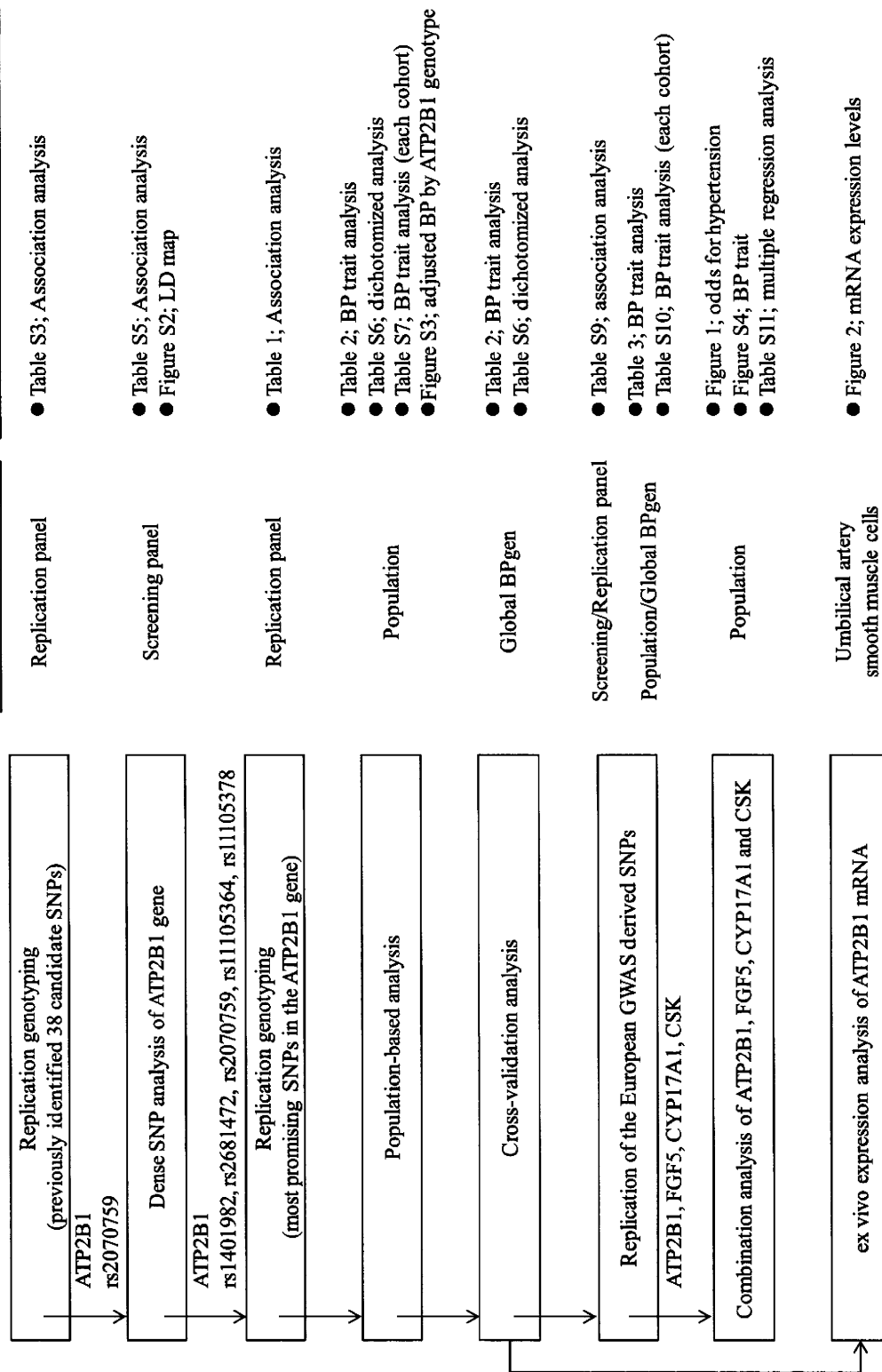


Figure S1 Study procedure and corresponding samples and results

FIGURE S2

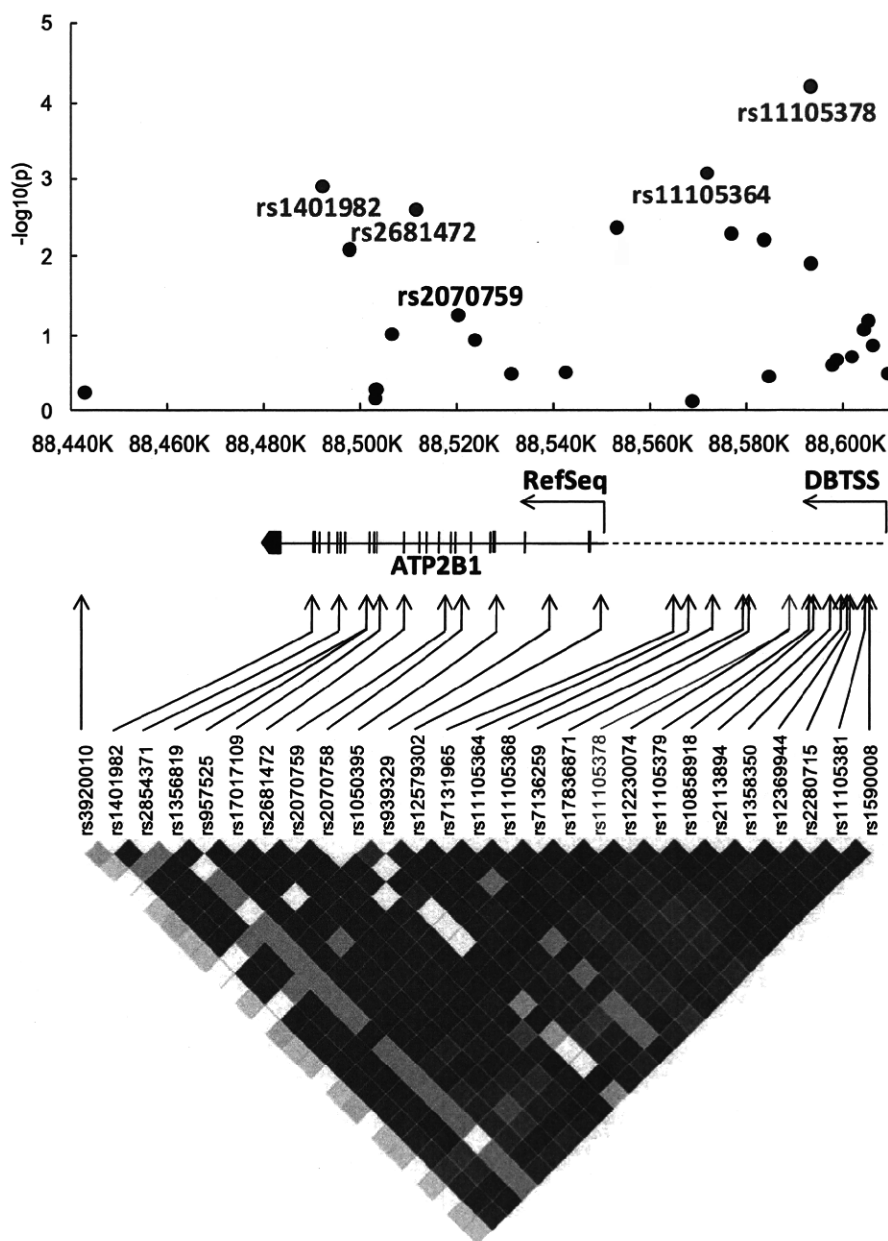


Figure S2 Dense SNP analysis of the ATP2B1 gene

The top graph shows p-values ($-\log_{10}(P)$) of association analyses using the screening panel (Table S4). The red circle (rs11105378) indicates the SNP showing the most significant association with hypertension. The lower panel shows a LD (D') map based on the genotype frequency of the control subjects