SUPPLEMENTARY INFORMATION

Common dysfunctional variants of *ABCG2* have stronger impact on hyperuricemia progression than typical environmental risk factors

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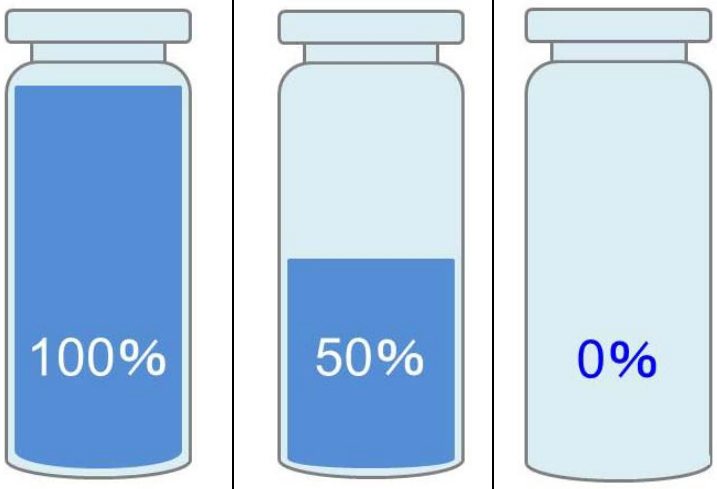
Supplementary Figure S1 | Diplotype of Q126X and Q141K alleles enables estimation of the urate-excretion function of ABCG2.

Supplementary Table S1 | Characteristics of 5,005 participants

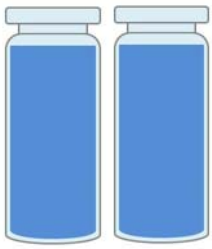
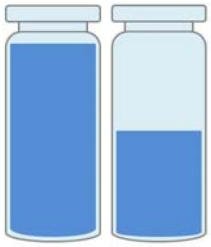
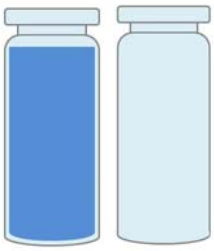
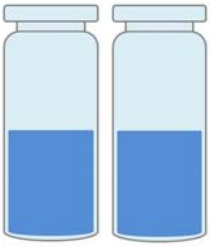
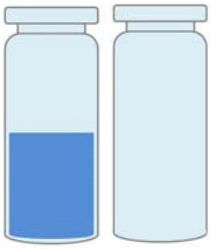
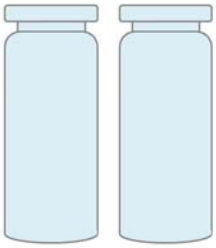
Supplementary Table S2 | SUA in each ABCG2 functional group

Supplementary Table S3 | Conversion table of alcohol consumption

a

Haplotype ID	*1	*2	*3
rs72552713 (Q126X)	126Q	126Q	126X
rs2231142 (Q141K)	141Q	141K	141Q
Relative function			

b

Diplotype	*1/*1 	*1/*2 	*1/*3  or *2/*2 	*2/*3  or *3/*3 
Estimated ABCG2 function	Full function	3/4 function	1/2 function	≤1/4 function

Supplementary Figure S1 | Diplotype of Q126X and Q141K alleles enables estimation of the urate-excretion function of ABCG2. (a) Since previous haplotype frequency analyses demonstrated no simultaneous presence of the minor alleles of Q126X and Q141K in one haplotype (references 8 and 10 in the main text), there are three kinds of haplotype (ABCG2*1, *2, and *3) with Q126X and Q141K alleles. ABCG2*1 shows a haplotype with neither Q141K nor Q126X variant, and ABCG2 *2 or *3 indicates a haplotype with Q141K or Q126X variant, respectively. Because Q141K and Q126X is a half-functional variant and a nonfunctional variant, respectively, relative function of ABCG2*1 ,*2, and *3 can be estimated as 100%, 50%, and 0%, which is visualized by the bins filled with water. (b) Each participant's function of urate exporter ABCG2 can be estimated from the diplotype, and can be also divided into four functional groups; ie., full function (normal function), 3/4 function (mild dysfunction), 1/2 function (moderate dysfunction) and ≤ 1/4 function (severe dysfunction). (This figure was modified from reference 11 in the main text, and produced by A.N. and H.M.)

Supplementary Table S1 | Characteristics of 5,005 Japanese participants

	Total	Male	Female
SUA (mg/dl)	5.57±0.02	6.10±0.02	4.44±0.02
Age (years)	52.3±0.12	52.8±0.15	51.2±0.22
BMI (kg/m^2)	23.0±0.04	23.5±0.05	22.0±0.08
Alcohol consumption (g/week of pure alcohol)	115.7±2.62	157.7±3.54	27.5±1.79

Abbreviations: SUA, serum uric acid. BMI, body mass index.

Results are expressed as means ± SE.

Supplementary Table S2 | SUA in each ABCG2 functional group

Function of ABCG2	Genotype combination (Q126X - Q141K)[†]	Diplotype of Q126X and Q141K[‡]	Total		Male		Female	
			N (%)	SUA (mg/dl)	*N* (%)	SUA (mg/dl)	*N* (%)	SUA (mg/dl)
Full function	C/C - C/C	*1/*1	2,307 (47.5)	5.41±0.03	1,561 (48.0)	5.92±0.03	746 (46.5)	4.34±0.03
3/4 function (mild dysfunction)	C/C - C/A	*1/*2	1,903 (39.2)	5.63±0.03	1,264 (38.9)	6.19±0.04	639 (39.8)	4.51±0.04
1/2 function (moderate dysfunction)	C/T - C/C C/C - A/A	*1/*3 *2/*2	574 (11.8)	5.71±0.06	379 (11.7)	6.31±0.06	195 (12.2)	4.54±0.08
≤1/4 function (severe dysfunction)	C/T - A/C T/T - C/C	*2/*3 *3/*3	73 (1.5)	5.98±0.16	49 (1.5)	6.51±0.17	24 (1.5)	4.88±0.21
total			4,857 (100.0)	5.54±0.02	3,253 (100.0)	6.08±0.02	1,604 (100.0)	4.44±0.02

Abbreviation: SUA, serum uric acid.

Unit of SUA is mg/dl. SUA is expressed as means ± SE.

[†]Risk alleles for Q126X (rs72552713) and Q141K (rs2231142) are underlined.

[‡]For the details of diplotype of Q126X and Q141K, see Supplementary Figure S1 and reference 11 (Matsuo, H. *et al.*, *Sci. Rep.* **4**, 3755 (2014)) of the main text.

Supplementary Table S3 | Conversion table of alcohol consumption

Alcoholic drinks	Amount	Alcohol consumption (grams of pure alcohol)
Whiskey	a single shot (= 30 ml)	10
	a double shot (= 60 ml)	20
Wine	a glass (=120 ml)	12
Beer	a large-sized bottle (= 633 ml)	25
	a mid-sized bottle (= 500 ml)	20
	a can of 350 ml (= 350 ml)	14
	a can of 250 ml (= 250 ml) or less	7
Japanese sake	1 gou (= 180 ml)	22
Shochu	1 gou (= 180 ml)	50
Shochu highball	1 glass (= 350 ml)	20