Supplementary Information

Meta-analysis identifies multiple loci associated with kidney function-related traits in East Asian populations

Yukinori Okada[1,2,40,*], Xueling Sim[3,4,40], Min Jin Go[5,40], Jer-Yuarn Wu[6,7,40], Dongfeng Gu[8,40], Fumihiko Takeuchi[9,40], Atsushi Takahashi[1], Shiro Maeda[10], Tatsuhiko Tsunoda[11], Peng Chen[12], Su-Chi Lim[12,13], Tien-Yin Wong[14,15,16], Jianjun Liu[17], Terri L. Young[18], Tin Aung[14,15], Mark Seielstad[19], Yik-Ying Teo[3,12,17,20,21], Young Jin Kim[5], Jong-Young Lee[5], Bok-Ghee Han[5], Daehee Kang[22], Chien-Hsiun Chen[6,7], Fuu-Jen Tsai[7], Li-Ching Chang[6], S.-J. Cathy Fann[6], Hao Mei[23], Dabeeru C. Rao[24], James E. Hixson[25], Shufeng Chen[8], Tomohiro Katsuya[26,27], Masato Isono[9], Toshio Ogihara[27,28], John C. Chambers[29], Weihua Zhang[29], Jaspal S. Kooner[30], the KidneyGen consortium[31], the CKDGen consortium[31], Eva Albrecht[32], the GUGC consortium[31], Kazuhiko Yamamoto[2], Michiaki Kubo[33], Yusuke Nakamura[34], Naoyuki Kamatani[35], Norihiro Kato[9,41], Jiang He[23,41], Yuan-Tsong Chen[6,41], Yoon Shin Cho[5,36,41], E-Shyong Tai[12,37,38,41], and Toshihiro Tanaka[39,41]

1. Laboratory for Statistical Analysis, Center for Genomic Medicine (CGM), RIKEN, Yokohama, Japan.
2. Department of Allergy and Rheumatology, Graduate School of Medicine, University of Tokyo, Tokyo, Japan.
3. Centre for Molecular Epidemiology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore.
4. Center for Statistical Genetics, University of Michigan, United States.
5. Center for Genome Science, National Institute of Health, Osong Health Technology Administration Complex, Chungcheongbuk-do, The Republic of Korea.
6. Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan.
7. School of Chinese Medicine, China Medical University, Taichung, Taiwan.
8. Cardiovascular Institute and Fu Wai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China.
9. Department of Gene Diagnostics and Therapeutics, Research Institute, National Center for Global Health and Medicine, Tokyo, Japan.
10. Laboratory for Endocrinology and Metabolism, CGM, RIKEN, Yokohama, Japan.
11. Laboratory for Medical Informatics, CGM, RIKEN, Yokohama, Japan.
12. Saw Swee Hock School of Public Health, National University of Singapore, Singapore.
13. Diabetes Centre and Department of Medicine, Khoo Teck Puat Hospital, Singapore.
14. Singapore Eye Research Institute, Singapore National Eye Centre, Singapore.

15. Department of Ophthalmology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore.
16. Centre for Eye Research Australia, University of Melbourne, East Melbourne VIC, Australia.
17. Genome Institute of Singapore, Agency for Science, Technology and Research, Singapore.
18. Center for Human Genetics, Duke University Medical Center, Durham, NC, USA.
19. Institute of Human Genetics, University of California, San Francisco, CA, USA.
20. Department of Statistics and Applied Probability, National University of Singapore, Singapore.
21. NUS Graduate School for Integrative Science and Engineering, National University of Singapore, Singapore.
22. Department of Preventive Medicine, Seoul National University College of Medicine, Seoul, The Republic of Korea.
23. Department of Epidemiology, Tulane University School of Public Health and Tropical Medicine, New Orleans, LA, USA.
24. Division of Biostatistics, Washington University School of Medicine, St. Louis, MO, USA.
25. Human Genetics Center, University of Texas School of Public Health, Houston, TX, USA.
26. Department of Clinical Gene Therapy, Osaka University Graduate School of Medicine, Suita, Japan.
27. Department of Geriatric Medicine and Nephrology, Osaka University Graduate School of Medicine, Suita, Japan.
28. Morinomiya University of Medical Sciences, Osaka, Japan.
29. Dept Epidemiology and Biostatistics, Imperial College London, United Kingdom.
30. National Heart and Lung Institute, Imperial College London, United Kingdom.
31. Full list of contributing authors for the KidneyGen, CKDGen, and GUGC consortia is provided in **Supplementary Information**.
32. Institute of Genetic Epidemiology, Helmholtz Zentrum München - German Research Center for Environmental Health, Neuherberg, Germany.
33. Laboratory for Genotyping Development, CGM, RIKEN, Yokohama, Japan.
34. Laboratory of Molecular Medicine, Human Genome Center, Institute of Medical Science, University of Tokyo, Tokyo, Japan.
35. Laboratory for International Alliance, CGM, RIKEN, Yokohama, Japan.
36. Department of Biomedical Science, Hallym University, Hallymdaehak-gil, Chuncheon, Gangwon-do, The Republic of Korea.
37. Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore, Singapore.
38. Duke-National University of Singapore Graduate Medical School, Singapore.

39. Laboratory for Cardiovascular Diseases, CGM, RIKEN, Yokohama, Japan.

40. These authors contributed equally to this work.

41. These authors directed equally to this work.

*****Corresponding author: Yukinori Okada

Laboratory for Statistical Analysis, Center for Genomic Medicine, RIKEN

4-6-1 Shirokane-dai, Minato-ku, Tokyo 108-8639, Japan

Telephone: +81-3-5449-5509, Fax: +81-3-5449-5564

E-mail: yokada@src.riken.jp

Section 1. Supplementary Tables.

Section 2. Supplementary Figures.

Section 3. Supplementary Note.

Section 1. Supplementary Tables

Supplementary Table 1. Characteristics of the cohorts enrolled in the GWAS meta-analysis and the replication study.

Stage	Cohort name	Study design	Ethnicity	Study name	Study participants	Reference
GWAS meta-analysis	The BioBank Japan Project (BBJ)	hospital-based	Japanese	BBJ_1 BBJ_2 BBJ_3 BBJ_4	unrelated patients affected with each of the 47 diseases	1-5
	Singapore Prospective Study Program (SP2)	population-based	Chinese	SP2_1 SP2_2 SP2_3	unrelated individuals	6-12
	Singapore Malay Eye Study (SiMES)		Malay	SiMES		
	Singapore Indian Eye Study (SINDI)		Indian	SINDI		
	Korea Association Resource project (KARE)	population-based	Korean	KARE	unrelated individuals	6,13,14
	Taiwan Super Control Study (TWSC) Taiwan Type 2 Diabetes Consortium (TWT2D)	population-based	Chinese	TWSC TWT2D	unrelated controls unrelated type II diabetes patients	6,15-17
	The Genetic Epidemiology Network of Salt Sensitivity (GenSalt)	family-based	Chinese	GenSalt	family-oriented individuals	6,18
	Cardio-metabolic Genome Epidemiology (CAGE)	hospital-based	Japanese	CAGE	unrelated individuals	6,19,20
Replication study	The BioBank Japan Project (BBJ)	hospital-based	Japanese	BBJ_5 BBJ_6	unrelated patients affected with each of the 47 diseases	- 21
	Singapore Chinese Eye Study (SCES)	population-based	Chinese	SCES	unrelated individuals	-
	Health Examinee shared control study (HEXA)	population-based	Korean	HEXA	unrelated individuals	14

GWAS, genome-wide association study.

Supplementary Table 2. Characteristics of the subjects enrolled in the GWAS meta-analysis and the replication study.

Stage	Study	No. subjects	No. subjects for each phenotype				Female	Age	Mean ± SD values of the traits			
			BUN	sCr	eGFRcrea[a]	UA	(%)	(mean±SD)	BUN (mg/dl)[b]	sCr (mg/dl)[b]	eGFRcrea (ml/min/1.73m^2)[b]	UA (mg/dl)[c]
GWAS meta-analysis	BBJ_1	23,542	22,258	23,356	23,536	14,286	45.6	62.7 ± 11.6	15.7 ± 6.3	0.76 ± 0.23	75.2 ± 21.0	5.32 ± 1.48
	BBJ_2	2,064	1,999	2,043	2,052	1,090	50.0	53.5 ± 14.5	14.1 ± 6.3	0.72± 0.20	82.9 ± 21.7	5.90 ± 1.90
	BBJ_3	1,056	1,048	1,055	1,055	872	100.0	36.3 ± 18.9	12.1 ± 4.2	0.60 ± 0.10	91.2 ± 18.0	5.32 ± 1.50
	BBJ_4	3,513	3,384	3,493	3,511	2,271	42.0	63.9 ± 9.1	15.2 ± 5.4	0.74 ± 0.20	77.2 ± 20.5	5.45 ± 1.52
	SP2_1	1,144	-	1,144	1,144	-	76.6	48.6 ± 11.4	-	0.82 ± 0.19	66.5 ± 14.6	-
	SP2_2	940	-	940	940	-	35.9	47.0 ± 10.4	-	0.95 ± 0.22	64.8 ± 13.0	-
	SP2_3	333	-	333	333	-	23.7	49.8 ± 12.8	-	0.95 ± 0.21	66.2 ± 14.4	-
	SiMES	2,521	-	2,521	2,521	-	50.5	59.0 ± 11.0	-	1.02 ± 0.30	55.3 ± 15.9	-
	SINDI	2,530	-	2,530	2,530	-	48.8	58.0 ± 10.0	-	0.87 ± 0.25	65.8 ± 16.1	-
	KARE	8,842	8,842	-	-	-	52.7	52.2 ± 8.9	14.4 ± 3.7	-	-	-
	TWSC	986	986	986	986	986	49.6	50.6 ± 17.4	16.8 ± 5.1	0.72 ± 0.19	84.8 ± 24.6	5.90 ± 1.79
	TWT2D	987	987	987	987	987	41.5	59.9 ± 10.3	17.9 ± 7.6	0.66 ± 0.26	105.0 ± 48.1	6.43 ± 1.70
	GenSalt	1,881	-	1,881	1,881	-	47.2	38.7 ± 9.5	-	0.95 ± 0.20	85.7 ± 20.3	-
	CAGE	988	213	988	975	925	62.5	69.5 ± 8.1	17.6 ± 6.7	0.74 ± 0.21	72.0 ±19.8	5.38 ± 1.31
Replication study	BBJ_5	11,952	11,524	11,844	11,819	7,174	46.2	59.1 ± 16.0	15.0 ± 4.9	0.75 ± 0	78.6 ± 22.4	5.39 ± 1.46
	BBJ_6	2,306	2,254	2,273	2,272	1,610	36.1	63.1 ± 12.5	16.2 ± 5.7	0.82 ± 0.25	71.7 ± 20.6	5.66 ± 1.47
	SCES	1,881	-	1,881	1881	-	51.3	58.4 ± 9.5	-	0.65± 0.27	97.0 ± 33.8	-
	HEXA	3,683	3,683	3,664	3,664	2,873	55.4	53.2 ± 8.3	14.0 ± 3.7	0.86 ± 0.21	87.9 ± 18.7	4.78 ± 1.32
GWAS meta-analysis		51,327	39,717	42,257	42,451	21,417	-	-	-	-	-	-
Replication study		19,822	17,461	19,662	19,636	11,657	-	-	-	-	-	-
Total		71,149	57,178	61,919	62,087	33,074	-	-	-	-	-	-

[a]Estimated based on serum creatinine levels using the Japanese coefficient-modified CKD Epidemiology Collaboration (CKD-EPI) equation[22].

[b]Common log-transformation was applied in the analysis.

[c]No transformation was applied in the analysis.

GWAS, genome-wide association study; BUN, blood urea nitrogen; sCr, serum creatinine; eGFRcrea, estimated glomerular filtration rate based on serum creatinine; UA, uric acid; SD, standard deviation.

Supplementary Table 3. Genotyping and imputation methods in the GWAS meta-analysis and the replication study.

Study	Typing platform	Quality control criteria				Imputation method				
		Sample call rate	SNP call rate	MAF	HWE *P*-value	Imputation software	MAF	Quality score	Analysis software	Reference panel
GWAS meta-analysis										
BBJ_1	Illumina HumanHap610-Quad Genotyping BeadChip	> 0.98	> 0.99	> 0.01	> 10^{-7}	MACH v1.0.16	> 0.01	*Rsq* > 0.5	mach2qtl	HapMap Phase II (rel24), JPT+CHB
BBJ_2	Illumina HumanHap550v3 Genotyping BeadChip	> 0.98	> 0.99	> 0.01	> 10^{-7}	MACH v1.0.16	> 0.01	*Rsq* > 0.5	mach2qtl	HapMap Phase II (rel24), JPT+CHB
BBJ_3	Illumina HumanHap550v3 Genotyping BeadChip	> 0.98	> 0.99	> 0.01	> 10^{-7}	MACH v1.0.16	> 0.01	*Rsq* > 0.5	mach2qtl	HapMap Phase II (rel24), JPT+CHB
BBJ_4	Illumina HumanOmniExpress Genotyping BeadChip	> 0.98	> 0.99	> 0.01	> 10^{-7}	MACH v1.0.16	> 0.01	*Rsq* > 0.5	mach2qtl	HapMap Phase II (rel24), JPT+CHB
SP2_1	Illumina HumanHap610-Quad Genotyping BeadChip	> 0.95	> 0.95	> 0.01	> 10^{-4}	IMPUTE v0.5.0	> 0.01	score-info >0.5	SNPTEST v2.1.1	HapMap Phase II (rel22), JPT+CHB
SP2_2	Illumina Human1M Genotyping BeadChip	> 0.95	> 0.95	> 0.01	> 10^{-4}	IMPUTE v0.5.0	> 0.01	score-info >0.5	SNPTEST v2.1.1	HapMap Phase II (rel22), JPT+CHB
SP2_3	Illumina HumanHap550 Genotyping BeadChip	> 0.95	> 0.95	> 0.01	> 10^{-4}	IMPUTE v0.5.0	> 0.01	score-info >0.5	SNPTEST v2.1.1	HapMap Phase II (rel22), JPT+CHB
SiMES	Illumina HumanHap610-Quad Genotyping BeadChip	> 0.95	> 0.95	> 0.01	> 10^{-6}	IMPUTE v0.5.0	> 0.01	score-info >0.5	SNPTEST v2.1.1	HapMap Phase II (rel22), 4 populations
SINDI	Illumina HumanHap610-Quad Genotyping BeadChip	> 0.95	> 0.95	> 0.01	> 10^{-6}	IMPUTE v0.5.0	> 0.01	score-info >0.5	SNPTEST v2.1.1	HapMap Phase II (rel22), 4 populations
KARE	Affymetrix Genome-wide Human Arrray 5.0	> 0.98	> 0.95	> 0.01	> 10^{-6}	IMPUTE	> 0.01	proper-info >0.5	PLINK	HapMap Phase II (rel22), JPT+CHB
TWSC	Illumina HumanHap550 Genotyping BeadChip	-	> 0.95	> 0.01	> 10^{-6}	IMPUTE v2	> 0.01	proper-info >0.5	SNPTEST v2	HapMap Phase II (rel22), JPT+CHB
TWT2D	Illumina HumanHap550 Genotyping BeadChip	-	> 0.95	> 0.01	> 10^{-6}	IMPUTE v2	> 0.01	proper-info >0.5	SNPTEST v2	HapMap Phase II (rel22), JPT+CHB
GenSalt	Affymetrix Genome-wide Human Arrray 6.0	-	> 0.75	> 0.01	> 10^{-7}	MACH 1.0.16	> 0.01	*Rsq* > 0.5	*R* v2.10.1	HapMap Phase II (rel22), JPT+CHB
CAGE	Illumina HumanHap610-Quad Genotyping BeadChip Illumina HumanHap550 Genotyping BeadChip	> 0.90	> 0.95	> 0.01	> 10^{-6}	BEAGLE v3.0.4	> 0.01	*Rsq* > 0.5	PLINK v1.06	HapMap Phase II (rel24), JPT+CHB
Replication study										
BBJ_5	Illumina HumanOmniExpress Genotyping BeadChip	> 0.98	> 0.99	> 0.01	> 10^{-7}	MACH v1.0.16	> 0.01	*Rsq* > 0.5	mach2qtl	HapMap Phase II (rel24), JPT+CHB
BBJ_6	Oligonucleotide array of Perlegen Sciences	> 0.95	> 0.95	> 0.01	> 10^{-6}	MACH v1.0.16	> 0.01	*Rsq* > 0.5	mach2qtl	HapMap Phase II (rel24), JPT+CHB
SCES	Illumina HumanHap610-Quad Genotyping BeadChip	> 0.95	> 0.95	> 0.01	> 10^{-6}	IMPUTE v0.5.0	> 0.01	score-info >0.5	SNPTEST v2.1.1	HapMap Phase II (rel22), JPT+CHB
HEXA	Affymetrix Genome-wide Human Arrray 6.0	> 0.98	> 0.95	> 0.01	> 10^{-6}	IMPUTE	> 0.01	proper-info >0.5	PLINK	HapMap Phase II (rel22), JPT+CHB

GWAS, genome-wide association study; MAF, minor allele frequency; HWE, Hardy-Weinberg equilibrium; JPT, Japanese; CHB, Han Chinese.

Supplementary Table 4. No. SNPs and inflation factors in the GWAS meta-analysis.

GWAS	No. SNPs				Inflation factor (λ_{GC})[a]			
	BUN	sCr	eGFRcrea	UA	BUN	sCr	eGFRcrea	UA
BBJ_1	2,263,308	2,263,308	2,263,308	2,263,308	1.042	1.065	1.062	1.028
BBJ_2	2,220,799	2,220,799	2,220,799	2,220,799	1.000	1.033	1.031	1.010
BBJ_3	2,220,799	2,220,799	2,220,799	2,220,799	1.014	1.003	1.012	0.994
BBJ_4	2,283,889	2,283,889	2,283,889	2,283,889	1.012	1.022	1.024	1.014
SP2_1	-	2,248,237	2,248,254	-	-	0.997	0.999	-
SP2_2	-	1,966,259	1,966,292	-	-	1.018	1.019	-
SP2_3	-	2,218,604	2,218,567	-	-	0.992	0.991	-
SiMES	-	1,982,211	1,982,204	-	-	0.998	0.998	-
SINDI	-	1,962,959	1,962,961	-	-	1.013	1.013	-
KARE	1,563,137	-	-	-	1.027	-	-	-
TWSC	2,159,680	2,159,647	2,159,672	2,159,674	1.002	1.008	1.004	0.993
TWT2D	2,159,636	2,159,593	2,159,608	2,159,630	1.003	1.005	0.999	1.009
GenSalt	-	1,060,441[b]	1,060,431[b]	-	-	1.031	1.017	-
CAGE	1,962,742	1,962,742	1,962,742	1,962,742	0.998	0.995	0.996	1.004
Meta-analysis[c]	2,281,523	2,353,587	2,353,587	2,278,301	1.060	1.072	1.079	1.031

[a]Genomic control corrections[23,24] were applied to each of the GWAS before the meta-analysis, and were applied again to the results of the meta-analysis. For the GWAS of which λ_{GC} were less than 1.00, genomic control corrections were not applied.

[b]We excluded SNPs in which generalized linear mixed models accounting for the family structures did not converge.

[c]SNPs that were evaluated in three or more GWAS were enrolled in the meta-analysis.

GWAS, genome-wide association study; BUN, blood urea nitrogen; sCr, serum creatinine; eGFRcrea, estimated glomerular filtration rate based on serum creatinine; UA, uric acid.

Nature Genetics: doi:10.1038/ng.2352

Supplementary Table 5. Results of the GWAS meta-analysis and the replication study for kidney function-related traits.

rsID[a]	Chr	Position (bp)	Band	Genes	A1/ A2[b]	Freq.[c]	Associations in East Asians						Associations in Europeans[e]		Ref.
							GWAS Meta-analysis		Replication study		Combined study				
							Beta (SE)[d]	*P*	Beta (SE)[d]	*P*	Beta (SE)[d]	*P*	Beta (SE)[f]	*P*	
Blood urea nitrogen (*n* = 39,717 for GWAS meta-analysis, *n* = 17,461 for replication)															
rs2049805	1	153,461,604	1q22	*MTX1-GBA*	T/C	0.17	0.0072 (0.0013)	1.9×10^{-8}	0.0072 (0.0017)	2.3×10^{-5}	0.0072 (0.0010)	1.8×10^{-12}			
rs11123170	2	113,695,411	2q13	*PAX8*	G/C	0.35	0.0059 (0.0010)	2.4×10^{-9}	0.0035 (0.0014)	0.014	0.0051 (0.0008)	3.3×10^{-10}			
rs13069000	3	66,881,640	3p14	*LRIG1-KBTBD8*	G/C	0.17	0.0097 (0.0013)	3.6×10^{-14}	0.0085 (0.0017)	4.8×10^{-7}	0.0093 (0.0010)	1.4×10^{-19}			2
rs16853722	3	170,633,326	3q26	*MECOM*	C/T	0.29	0.0059 (0.0010)	1.3×10^{-8}	0.0072 (0.0014)	2.7×10^{-7}	0.0064 (0.0008)	2.7×10^{-14}			
rs10937329	3	189,196,412	3q27	*BCL6-LPP*	T/A	0.69	0.0103 (0.0010)	8.4×10^{-24}	0.0092 (0.0017)	1.0×10^{-7}	0.0100 (0.0009)	8.8×10^{-30}			2
rs17663555	5	72,467,792	5q13	*TMEM171-TMEM174*	G/C	0.34	0.0046 (0.0010)	3.9×10^{-6}	0.0026 (0.0015)	0.093	0.0040 (0.0008)	1.8×10^{-6}			
rs2206271	6	50,893,967	6p12	*TFAP2B*	A/T	0.32	0.0066 (0.0014)	1.3×10^{-6}	0.0039 (0.0016)	0.016	0.0055 (0.0010)	1.6×10^{-7}			
rs1936800	6	127,477,757	6q22	*RSPO3*	T/C	0.50	0.0049 (0.0009)	1.7×10^{-7}	0.0056 (0.0013)	1.7×10^{-5}	0.0052 (0.0008)	1.2×10^{-11}			14
rs10275044	7	1,240,371	7p22	*UNCX*	T/A	0.34	0.0079 (0.0015)	1.3×10^{-7}	0.0053 (0.0019)	0.0056	0.0069 (0.0012)	4.3×10^{-9}			
rs17169194	7	7,647,222	7p21	*RPA3*	A/C	0.89	0.0088 (0.0019)	1.9×10^{-6}	0.0003 (0.0024)	0.92	0.0055 (0.0015)	1.4×10^{-4}			
rs10984991	9	122,513,063	9q33	*MEGF9*	A/G	0.11	0.0089 (0.0018)	7.1×10^{-7}	-0.0011 (0.0023)	0.62	0.0051 (0.0014)	3.0×10^{-4}			
rs10767873	11	30,725,254	11p14	*MPPED2-DCDC5*	C/T	0.69	0.0068 (0.0010)	7.0×10^{-11}	0.0068 (0.0014)	1.4×10^{-6}	0.0068 (0.0008)	4.5×10^{-16}			
rs2074356	12	111,129,784	12q24.13	*C12orf51*	A/G	0.23	0.0064 (0.0013)	4.4×10^{-7}	0.0063 (0.0020)	0.0012	0.0064 (0.0011)	1.8×10^{-9}			
rs17730281	15	51,695,240	15q21	*WDR72*	G/A	0.58	0.0054 (0.0010)	1.5×10^{-8}	0.0046 (0.0013)	4.5×10^{-4}	0.0051 (0.0008)	3.0×10^{-11}			
rs11868441	17	56,594,003	17q23	*BCAS3*	G/A	0.75	0.0062 (0.0013)	2.1×10^{-6}	0.0055 (0.0015)	2.2×10^{-4}	0.0059 (0.0010)	2.1×10^{-9}			
rs7227483	18	41,441,128	18q12	*SLC14A2*	G/A	0.80	0.0086 (0.0012)	1.0×10^{-12}	0.0078 (0.0016)	9.6×10^{-7}	0.0083 (0.0010)	6.7×10^{-18}			2
rs6026584	20	56,902,468	20q13	*GNAS*	T/C	0.32	0.0055 (0.0011)	7.1×10^{-7}	0.0046 (0.0016)	0.0033	0.0052 (0.0009)	8.8×10^{-9}			
Serum creatinine (*n* = 42,257 for GWAS meta-analysis, *n* = 19,662 for replication, *n* = 23,812 for Europeans[25])															
rs13146355	4	77,631,164	4q21	*SHROOM3*	A/G	0.21	0.0052 (0.0009)	3.6×10^{-9}	0.0039 (0.0011)	5.3×10^{-4}	0.0047 (0.0007)	9.4×10^{-12}	0.0031 (0.0006)	7.7×10^{-7}	25
rs12654812	5	176,726,797	5q35	*RGS14*	A/G	0.36	0.0049 (0.0009)	3.2×10^{-8}	0.0011 (0.0013)	0.37	0.0036 (0.0007)	4.8×10^{-7}			
rs3828890	6	31,548,648	6p21	MHC region	G/C	0.11	0.0074 (0.0015)	5.3×10^{-7}	0.0060 (0.0018)	0.0011	0.0069 (0.0012)	2.6×10^{-9}	N.A.	N.A.	
rs17757177	6	55,402,974	6p12	*RBM16*	A/C	0.24	0.0041 (0.0009)	1.8×10^{-6}	-0.0011 (0.0011)	0.35	0.0022 (0.0007)	1.2×10^{-3}			
rs4870304	6	155,033,535	6q25	*CNKSR3-RBM16*	G/A	0.29	0.0038 (0.0008)	9.1×10^{-7}	-0.0002 (0.0013)	0.91	0.0028 (0.0007)	2.6×10^{-5}			
rs10277115	7	1,251,721	7p22	*UNCX*	T/A	0.35	0.0060 (0.0009)	2.2×10^{-10}	0.0034 (0.0015)	0.022	0.0052 (0.0008)	4.6×10^{-11}	0.0011 (0.0013)	0.41	
rs963837	11	30,705,666	11p14	*MPPED2-DCDC5*	T/C	0.64	0.0036 (0.0007)	7.5×10^{-7}	0.0040 (0.0012)	0.0013	0.0037 (0.0006)	3.4×10^{-9}	0.0007 (0.0006)	0.25	
rs671	12	110,726,149	12q24.2	*ALDH2*	A/G	0.27	0.0047 (0.0009)	5.0×10^{-8}	0.0040 (0.0013)	0.0015	0.0045 (0.0007)	2.8×10^{-10}	N.A.	N.A.	
rs17778975	13	108,621,111	13q33	*MYO16*	A/T	0.78	0.0051 (0.0011)	4.9×10^{-6}	-0.0003 (0.0018)	0.88	0.0036 (0.0010)	1.6×10^{-4}			
rs2470171	15	49,453,614	15q21	*GLDN*	T/C	0.42	0.0035 (0.0008)	4.4×10^{-6}	0.0004 (0.0010)	0.68	0.0024 (0.0006)	8.8×10^{-5}			
rs17730436	15	51,730,220	15q21	*WDR72*	T/C	0.60	0.0046 (0.0008)	2.4×10^{-8}	0.0058 (0.0012)	7.3×10^{-7}	0.0050 (0.0007)	1.2×10^{-13}	N.A.	N.A.	2
rs11864909	16	20,308,340	16p12	*UMOD*	C/T	0.81	0.0055 (0.0009)	4.8×10^{-9}	0.0044 (0.0016)	0.0050	0.0052 (0.0008)	1.1×10^{-10}	0.0040 (0.0009)	5.6×10^{-6}	26
rs181533	17	8,750,557	17p13	*PIK3R5*	T/C	0.79	0.0056 (0.0012)	1.3×10^{-6}	0.0008 (0.0016)	0.63	0.0039 (0.0009)	2.8×10^{-5}			
rs9895661	17	56,811,371	17q23	*BCAS3*	C/T	0.52	0.0047 (0.0008)	1.1×10^{-8}	0.0039 (0.0012)	0.0018	0.0045 (0.0007)	7.4×10^{-11}	0.0046 (0.0009)	2.4×10^{-6}	25

eGFRcrea (*n* = 42,451 for GWAS meta-analysis, *n* = 19,636 for replication, *n* = 67,093 for Europeans[27])															
rs7649443	3	198,416,218	3q29	*DLG1*	C/T	0.72	-0.0045 (0.0010)	2.6×10^{-6}	0.0016 (0.0014)	0.26	-0.0025 (0.0008)	1.3×10^{-3}			
rs13146355	4	77,631,164	4q21	*SHROOM3*	A/G	0.21	-0.0056 (0.0010)	2.7×10^{-8}	-0.0043 (0.0012)	5.0×10^{-4}	-0.0051 (0.0008)	6.6×10^{-11}	-0.0117 (0.0013)	$2,0\times10^{-17}$	27,28
rs12654812	5	176,726,797	5q35	*RGS14*	A/G	0.36	-0.0056 (0.0010)	2.9×10^{-8}	-0.0016 (0.0014)	0.25	-0.0042 (0.0008)	2.3×10^{-7}			27
rs3828890	6	31,548,648	6p21	MHC region	G/C	0.11	-0.0091 (0.0017)	9.8×10^{-8}	-0.0062 (0.0020)	0.0018	-0.0079 (0.0013)	1.2×10^{-9}	N.A.	N.A.	
rs17757177	6	55,402,974	6p12	*RBM16*	A/C	0.24	-0.0046 (0.0010)	3.7×10^{-6}	0.0011 (0.0012)	0.36	-0.0023 (0.0008)	2.6×10^{-3}			
rs2797369	6	101,781,011	6q16	*GRIK2*	T/C	0.66	-0.0046 (0.0010)	4.5×10^{-6}	-0.0036 (0.0013)	0.0069	-0.0042 (0.0008)	1.1×10^{-7}			
rs9397738	6	155,028,356	6q25	*CNKSR3-RBM16*	G/A	0.22	-0.0048 (0.0010)	1.4×10^{-6}	-0.0014 (0.0016)	0.37	-0.0039 (0.0009)	4.9×10^{-6}			
rs10277115	7	1,251,721	7p22	*UNCX*	T/A	0.35	-0.0066 (0.0011)	7.3×10^{-10}	-0.0039 (0.0016)	0.014	-0.0058 (0.0009)	1.0×10^{-10}	-0.0055 (0.0022)	0.016	
rs963837	11	30,705,666	11p14	*MPPED2-DCDC5*	T/C	0.64	-0.0041 (0.0008)	6.3×10^{-7}	-0.0048 (0.0013)	3.8×10^{-4}	-0.0043 (0.0007)	1.1×10^{-9}	-0.0074 (0.0013)	5.3×10^{-8}	
rs17778975	13	108,621,111	13q33	*MYO16*	A/T	0.78	-0.0061 (0.0013)	1.7×10^{-6}	0.0003 (0.0020)	0.90	-0.0042 (0.0011)	7.5×10^{-5}			
rs17730436	15	51,730,220	15q21	*WDR72*	T/C	0.60	-0.0053 (0.0010)	3.0×10^{-8}	-0.0061 (0.0013)	1.4×10^{-6}	-0.0055 (0.0008)	6.0×10^{-13}	-0.0092 (0.0071)	0.22	
rs11864909	16	20,308,340	16p12	*UMOD*	C/T	0.81	-0.0062 (0.0011)	9.1×10^{-9}	-0.0044 (0.0017)	0.0085	-0.0057 (0.0009)	3.6×10^{-10}	-0.0118 (0.0016)	1.0×10^{-12}	27,28
rs438835	17	8,744,849	17p13	*PIK3R5*	C/A	0.77	-0.0055 (0.0012)	3.1×10^{-6}	-0.0002 (0.0016)	0.91	-0.0036 (0.0010)	1.3×10^{-4}			
rs9895661	17	56,811,371	17q23	*BCAS3*	C/T	0.52	-0.0053 (0.0009)	1.9×10^{-8}	-0.0046 (0.0014)	5.8×10^{-4}	-0.0051 (0.0008)	4.8×10^{-11}	-0.0105 (0.0018)	1.4×10^{-8}	27
Urate (*n* = 21,417 for GWAS meta-analysis, *n* = 11,657 for replication, *n* = 110,347 for Europeans[29])															
rs1021916	2	212,841,067	2q34	*ERBB4*	G/A	0.84	0.0965 (0.0199)	1.2×10^{-6}	0.0201 (0.0229)	0.38	0.0637 (0.0150)	2.2×10^{-5}			
rs10513699	3	173,475,606	3q26	*FNDC3B*	G/T	0.92	0.1152 (0.0236)	1.0×10^{-6}	-0.0315 (0.0322)	0.33	0.0640 (0.0190)	7.6×10^{-4}			
rs3775948	4	9,604,280	4p16	*SLC2A9*	C/G	0.59	0.1860 (0.0135)	2.9×10^{-43}	0.1674 (0.0165)	3.6×10^{-24}	0.1786 (0.0104)	1.6×10^{-65}	0.3555 (0.0061)	$< 10^{-600}$	2,30-36
rs2725220	4	89,178,946	4q22	*ABCG2*	C/G	0.32	0.1363 (0.0144)	2.2×10^{-21}	0.1323 (0.0210)	2.8×10^{-10}	0.1350 (0.0118)	4.2×10^{-30}	0.0154 (0.0055)	0.0076	2,33,35,36
rs504915	11	64,220,661	11q13	*SLC22A12*	T/A	0.82	0.2567 (0.0177)	9.4×10^{-48}	0.1822 (0.0206)	8.7×10^{-19}	0.2251 (0.0134)	3.3×10^{-63}	0.0619 (0.0059)	1.6×10^{-23}	2,35,36
rs889472	16	78,203,490	16q23	*MAF*	C/A	0.57	0.0758 (0.0136)	2.8×10^{-8}	0.0584 (0.0227)	0.010	0.0711 (0.0117)	1.1×10^{-9}	0.0079 (0.0062)	0.23	

[a]SNPs that satisfied $P < 5.0 \times 10^{-6}$ in the GWAS meta-analysis are indicated.

[b]The allele that increased blood urea nitrogen, serum creatinine, and uric acid or that decreased eGFRcrea was denoted as allele 1 (A1) and indicated on the basis of the forward strand of the NCBI build 36.

[c]Frequency of allele 1 in the GWAS meta-analysis.

[d]Effect size of allele 1 on common log-transformed values of blood urea nitrogen, serum creatinine, and eGFRcrea, or non-transformed values of uric acid.

[e]SNPs that satisfied $P < 5.0 \times 10^{-8}$ in the combined study of GWAS meta-analysis and replication study for serum creatinine, eGFRcrea, or uric acid were evaluated using the results of the European studies, as described elsewhere[25,27,29].

[f]Effect size of allele 1 on % change in serum creatinine, natural log-transformed values of eGFRcrea, or non-transformed values of uric acid.

GWAS, genome-wide association study; SE, standard error; eGFRcrea, estimated glomerular filtration rate based on serum creatinine; N.A., not available.

Supplementary Table 6. Correlations among the kidney function-related traits.

		r			
		BUN	sCr	eGFRcrea	UA
R^2	BUN	-	0.452	-0.500	0.249
	sCr	0.205	-	-0.875	0.483
	eGFRcrea	0.250	0.765	-	-0.365
	UA	0.062	0.234	0.133	-

The correlation coefficient, *r*, and the coefficient of determination, R^2, between each pair of the values of the kidney function-related traits estimated using the Japanese subjects from the BioBank Japan Project enrolled in the GWAS meta-analysis (BBJ_1-4; *n* = 30,175) are indicated.

For BUN, sCr, and eGFRcrea, correlations for common log-transformed values were evaluated.

BUN, blood urea nitrogen; sCr, serum creatinine; eGFRcrea, estimated glomerular filtration rate based on serum creatinine; UA, uric acid.

Supplementary Table 7. Associations in the previously reported loci associated with kidney function-related traits.

Associations of the previously reported SNPs								Associations of the best SNPs in East Asians			
rsID	Chr	Position (bp)	Cytoband	Genes	A1/A2[a]	Freq.	Beta (SE)[b]	*P*	rsID[c]	Chr	Position (bp)	*P*
Blood urea nitrogen (*n* = 39,717)												
rs11709625	3	66,905,847	3p14	*LRIG1-KBTBD8*	A/C	0.17	0.0095 (0.0013)	2.7×10^{-13}	rs13069000	3	66,881,640	3.6×10^{-14}
rs9820070	3	189,169,768	3q27	*BCL6-LPP*	A/C	0.68	0.0098 (0.0010)	5.2×10^{-23}	rs10937329	3	189,196,412	8.4×10^{-24}
rs6569474	6	127,535,304	6q22	*RSPO3*	A/T	0.50	-0.0038 (0.0010)	4.8×10^{-5}	rs1936800	6	127,477,757	1.7×10^{-7}
rs7227483	18	41,441,128	18q12	*SLC14A2*	A/G	0.20	-0.0086 (0.0012)	1.0×10^{-12}	rs7227483	18	41,441,128	1.0×10^{-12}
Serum creatinine (*n* = 42,257)												
rs10206899	2	73,754,408	2p13	*NAT8*	T/C	0.94	0.0046 (0.0041)	0.26			-	
rs9992101	4	77,579,455	4q21	*SHROOM3*	A/G	0.092	0.0048 (0.0014)	3.4×10^{-4}	rs13146355	4	77,631,164	3.6×10^{-9}
rs3127573	6	160,601,383	6q25	*SLC22A2*	A/G	0.92	-0.0021 (0.0013)	0.12			-	
rs10518733	15	51,727,599	15q21	*WDR72*	A/C	0.60	0.0038 (0.0007)	1.4×10^{-7}	rs17730436	15	51,730,220	2.4×10^{-8}
rs4293393	16	20,272,089	16p12	*UMOD*	A/G	0.89	0.0021 (0.0013)	0.11			-	
rs8068318	17	56,838,548	17q23	*TBX2*	T/C	0.37	-0.0019 (0.0008)	0.012			-	
rs4805834	19	38,145,499	19q13	*SLC7A9*	T/C	0.090	0.0006 (0.0012)	0.63			-	
eGFRcrea (*n* = 42,451)												
rs1933182	1	109,801,361	1p13	*PSMA5-SYPL2*	A/C	0.090	0.0015 (0.0021)	0.48			-	
rs267734	1	149,218,101	1q21	*LASS2-ANXA9*	T/C	0.92	-0.0015 (0.0021)	0.48			-	
rs1260326	2	27,584,444	2p23	*GCKR*	T/C	0.52	0.0017 (0.0008)	0.039			-	
rs13538	2	73,721,836	2p13	*NAT8*	G/A	0.00	-				-	
rs7422339	2	211,248,752	2q34	*CPS1*	A/C	0.19	-0.0050 (0.0012)	4.9×10^{-5}	rs4567871	2	211,247,547	5.1×10^{-5}
rs347685	3	143,289,827	3q23	*TFDP2*	A/C	0.72	-0.0011 (0.0009)	0.26			-	
rs17319721	4	77,587,871	4q21	*SHROOM3*	A/G	0.083	-0.0060 (0.0015)	8.3×10^{-5}	rs13146355	4	77,631,164	2.7×10^{-8}
rs11959928	5	39,432,889	5p13	*DAB2*	A/T	0.25	-0.0003 (0.0010)	0.74			-	
rs6420094	5	176,750,242	5q35	*RGS14*	A/G	0.71	0.0044 (0.0009)	7.5×10^{-7}	rs12654812	5	176,726,797	2.9×10^{-8}
rs881858	6	43,914,587	6p21	*VEGFA*	A/G	0.72	0.0001 (0.0019)	0.94			-	
rs2279463	6	160,588,379	6q25	*SLC22A2*	A/G	0.89	0.0005 (0.0016)	0.75			-	
rs6465825	7	77,254,375	7q11	*RSBN1L-TMEM60*	T/C	0.76	0.0021 (0.0010)	0.028			-	
rs10109414	8	23,807,096	8p21	*STC1*	T/C	0.20	-0.0035 (0.0010)	6.4×10^{-4}	rs6982337	8	23,750,432	2.6×10^{-5}
rs4744712	9	70,624,527	9q21	*PIP5K1B*	A/C	0.38	-0.0017 (0.0008)	0.047			-	
rs10794720	10	1,146,165	10p15	*WDR37*	T/C	0.11	-0.0016 (0.0015)	0.28			-	
rs4014195	11	65,263,398	11q13	*RNASEH2C-OVOL1*	G/C	0.20	-0.0042 (0.0010)	4.6×10^{-5}	rs12576996	11	65,337,214	1.6×10^{-5}
rs10774021	12	219,559	12p13	*SLC6A13*	T/C	0.34	-0.0031 (0.0009)	3.9×10^{-4}	rs7969761	12	226,103	1.9×10^{-5}
rs626277	13	71,245,697	13q21	*DACH1*	A/C	0.19	-0.0028 (0.0011)	0.013			-	
rs2453533	15	43,428,517	15q21	*GATM-SPATA5L1*	A/C	0.87	-0.0035 (0.0014)	0.016			-	
rs491567	15	51,733,885	15q21	*WDR72*	A/C	0.53	-0.0037 (0.0008)	4.7×10^{-6}	rs17730436	15	51,730,220	3.0×10^{-8}
rs1394125	15	73,946,038	15q24	*UBE2Q2*	A/G	0.091	-0.0016 (0.0014)	0.26			-	
rs4293393	16	20,272,089	16p12	*UMOD-PDILT*	A/G	0.89	-0.0027 (0.0015)	0.083			-	
rs9895661	17	56,811,371	17q23	*BCAS3*	T/C	0.48	0.0057 (0.0009)	1.8×10^{-9}	rs9895661	17	56,811,371	1.9×10^{-8}
rs12460876	19	38,048,731	19q13	*SLC7A9*	T/C	0.38	-0.0011 (0.0008)	0.20			-	
Urate (*n* = 21,417)												
rs12129861	1	144,437,046	1q21	*PDZK1*	A/G	0.13	-0.064 (0.021)	0.0020				
rs780093	2	27,596,107	2p23	*GCKR*	T/C	0.55	0.045 (0.013)	8.7×10^{-4}	rs4665987	2	27,609,329	8.8×10^{-5}
rs2544390	2	169,913,092	2q31	*LRP2*	T/C	0.49	0.052 (0.013)	1.1×10^{-4}	rs2673172	2	169,913,046	8.1×10^{-5}
rs13129697	4	9,536,065	4p16	*SLC2A9*	T/G	0.52	0.130 (0.013)	4.2×10^{-22}	rs3775948	4	9,604,280	2.9×10^{-43}
rs4148155	4	89,273,691	4q22	*ABCG2*	A/G	0.70	-0.168 (0.015)	1.6×10^{-20}	rs2725220	4	89,178,946	2.2×10^{-21}
rs675209	6	7,047,083	6p24	*RREB1*	T/C	0.93	0.043 (0.026)	0.10			-	
rs1183201	6	25,931,423	6p22	*LRRC16A-SLC17A1*	A/T	0.16	-0.065 (0.018)	2.6×10^{-4}	rs566530	6	25,986,340	4.9×10^{-5}
rs12356193	10	61,083,359	10q21	*SLC16A9*	G/A	0.00	-				-	
rs506338	11	64,197,496	11q13	*SLC22A12*	T/C	0.82	0.253 (0.018)	5.6×10^{-47}	rs504915	11	64,220,661	9.4×10^{-48}
rs1106766	12	56,095,723	12q13	*INHBC*	T/C	0.077	-0.005 (0.027)	0.86			-	

[a]On the basis of the forward strand of the NCBI build 36.

[b]Effect size of allele 1 on common log-transformed blood urea nitrogen, serum creatinine, and eGFRcrea levels, or non-transformed uric acid levels in the GWAS meta-analysis.

[c]For the SNP that were significantly replicated in our East Asian subjects($P < 0.0016$), the most associated SNP in the East Asian subjects located ± 200kb of the SNP reported in the previous study was indicated.

SE, standard error.

Supplementary Table 8. Pleiotropic associations of the identified loci among the kidney function-related traits and risk of chronic kidney disease.

rsID	Chr	Position (bp)	Band	Genes	A1/A2[a]	Blood urea nitrogen (*n* = 57,178)		Serum creatinine (*n* = 61,919)		eGFRcrea (*n* = 62,087)		Uric acid (*n* = 33,074)		Chronic kidney disease (8,805 cases and 35,259 controls)	
						Beta (SE)[b]	*P* [d]	Beta (SE)[b]	*P* [d]	Beta (SE)[b]	*P* [d]	Beta (SE)[b]	*P* [d]	OR (95%CI)[c]	*P* [d]
rs2049805	1	153,461,604	1q22	*MTX1-GBA*	T/C	0.0072 (0.0010)	**1.8×10^{-12}**	0.0016 (0.0007)	0.027	-0.0016 (0.0008)	0.046	0.042 (0.014)	**0.0022**	0.99 (0.95-1.04)	0.75
rs11123170	2	113,695,411	2q13	*PAX8*	G/C	0.0051 (0.0008)	**3.3×10^{-10}**	0.0017 (0.0006)	0.0059	-0.0018 (0.0007)	0.0082	0.020 (0.011)	0.079	1.06 (1.02-1.10)	0.0058
rs13069000	3	66,881,640	3p14	*LRIG1-KBTBD8*	G/C	0.0093 (0.0010)	**1.4×10^{-19}**	0.0009 (0.0008)	0.24	-0.0007 (0.0009)	0.42	0.037 (0.014)	0.0093	1.00 (0.95-1.05)	0.94
rs16853722	3	170,633,326	3q26	*MECOM*	T/C	-0.0064 (0.0008)	**2.7×10^{-14}**	-0.0022 (0.0007)	**9.4×10^{-4}**	0.0024 (0.0007)	**8.3×10^{-4}**	-0.004 (0.012)	0.76	0.94 (0.90-0.97)	**9.9×10^{-4}**
rs10937329	3	189,196,412	3q27	*BCL6-LPP*	A/T	-0.0100 (0.0009)	**8.8×10^{-30}**	-0.0001 (0.0007)	0.90	-0.0001 (0.0008)	0.93	-0.012 (0.013)	0.36	1.02 (0.98-1.06)	0.40
rs3775948	4	9,604,280	4p16	*SLC2A9*	G/C	0.0015 (0.0008)	0.061	-0.0005 (0.0006)	0.40	0.0006 (0.0006)	0.36	-0.179 (0.010)	**1.6×10^{-65}**	0.97 (0.94-1.01)	0.13
rs13146355	4	77,631,164	4q21	*SHROOM3*	A/G	0.0018 (0.0009)	0.043	0.0047 (0.0007)	**9.4×10^{-12}**	-0.0051 (0.0008)	**6.6×10^{-11}**	0.017 (0.012)	0.16	1.04 (0.99-1.08)	0.090
rs2725220	4	89,178,946	4q22	*ABCG2*	G/C	0.0011 (0.0009)	0.20	-0.0009 (0.0007)	0.18	0.0009 (0.0007)	0.23	-0.135 (0.012)	**4.2×10^{-30}**	0.99 (0.95-1.02)	0.44
rs3828890	6	31,548,648	6p21	MHC region	G/C	0.0021 (0.0014)	0.14	0.0069 (0.0012)	**2.6×10^{-9}**	-0.0079 (0.0013)	**1.2×10^{-9}**	0.038 (0.020)	0.051	1.11 (1.04-1.19)	**0.0016**
rs1936800	6	127,477,757	6q22	*RSPO3*	T/C	0.0052 (0.0008)	**1.2×10^{-11}**	-0.0003 (0.0006)	0.64	0.0004 (0.0007)	0.57	-0.003 (0.010)	0.78	1.01 (0.97-1.04)	0.72
rs10277115	7	1,251,721	7p22	*UNCX*	A/T	-0.0072 (0.0012)	**1.9×10^{-9}**	-0.0052 (0.0008)	**4.6×10^{-11}**	0.0058 (0.0009)	**1.0×10^{-10}**	-0.036 (0.015)	0.014	0.89 (0.85-0.93)	**1.7×10^{-6}**
rs10767873	11	30,725,254	11p14	*MPPED2-DCDC5*	T/C	-0.0068 (0.0008)	**4.5×10^{-16}**	-0.0033 (0.0007)	**4.3×10^{-7}**	0.0038 (0.0007)	**1.8×10^{-7}**	-0.029 (0.012)	0.012	0.94 (0.91-0.98)	0.0055
rs504915	11	64,220,661	11q13	*SLC22A12*	A/T	-0.0005 (0.0011)	0.68	0.0007 (0.0007)	0.32	-0.0007 (0.0008)	0.39	-0.225 (0.013)	**3.3×10^{-63}**	0.99 (0.95-1.04)	0.74
rs671	12	110,726,149	12q24.2	*ALDH2*	A/G	0.0045 (0.0010)	**1.3×10^{-5}**	0.0045 (0.0007)	**2.8×10^{-10}**	-0.0043 (0.0008)	**7.8×10^{-8}**	-0.062 (0.013)	**1.6×10^{-6}**	1.03 (0.99-1.08)	0.16
rs2074356	12	111,129,784	12q24.13	*C12orf51*	A/G	0.0064 (0.0011)	**1.8×10^{-9}**	0.0049 (0.0008)	**1.9×10^{-9}**	-0.0050 (0.0009)	**6.5×10^{-8}**	-0.064 (0.015)	**1.6×10^{-5}**	1.04 (0.99-1.09)	0.14
rs17730281	15	51,695,240	15q21	*WDR72*	A/G	-0.0051 (0.0008)	**3.0×10^{-11}**	-0.0044 (0.0006)	**3.6×10^{-14}**	0.0049 (0.0007)	**1.3×10^{-13}**	-0.011 (0.010)	0.29	0.90 (0.87-0.93)	**1.3×10^{-8}**
rs11864909	16	20,308,340	16p12	*UMOD*	T/C	-0.0034 (0.0012)	0.0058	-0.0052 (0.0008)	**1.1×10^{-10}**	0.0057 (0.0009)	**3.6×10^{-10}**	-0.002 (0.015)	0.87	0.92 (0.87-0.96)	**7.0×10^{-4}**
rs889472	16	78,203,490	16q23	*MAF*	A/C	-0.0010 (0.0010)	0.30	-0.0007 (0.0006)	0.29	0.0007 (0.0007)	0.30	-0.071 (0.012)	**1.1×10^{-9}**	0.94 (0.90-0.97)	**0.0012**
rs11868441	17	56,594,003	17q23	*BCAS3*	A/G	-0.0059 (0.0010)	**2.1×10^{-9}**	-0.0017 (0.0007)	0.010	0.0019 (0.0008)	0.0098	0.032 (0.012)	0.0089	0.96 (0.92-1.00)	0.062
rs9895661	17	56,811,371	17q23	*BCAS3*	T/C	-0.0005 (0.0010)	0.65	-0.0045 (0.0007)	**7.4×10^{-11}**	0.0051 (0.0008)	**4.8×10^{-11}**	0.042 (0.013)	**9.3×10^{-4}**	0.94 (0.90-0.98)	0.0060
rs7227483	18	41,441,128	18q12	*SLC14A2*	A/G	-0.0083 (0.0010)	**6.7×10^{-18}**	0.0008 (0.0008)	0.32	-0.0009 (0.0009)	0.32	0.028 (0.013)	0.033	1.04 (0.99-1.08)	0.11
rs6026584	20	56,902,468	20q13	*GNAS*	T/C	0.0052 (0.0009)	**8.8×10^{-9}**	0.0010 (0.0007)	0.19	-0.0013 (0.0008)	0.10	0.037 (0.013)	0.0041	1.07 (1.02-1.12)	**0.0022**

[a]Indicated on the basis of the forward strand of the NCBI build 36.

[b]Effect size of allele 1 on common log-transformed blood urea nitrogen, serum creatinine, and eGFRcrea levels, or non-transformed uric acid levels in the combined study of the GWAS meta-analysis and the replication study.

[c]Odds ratio of allele 1.

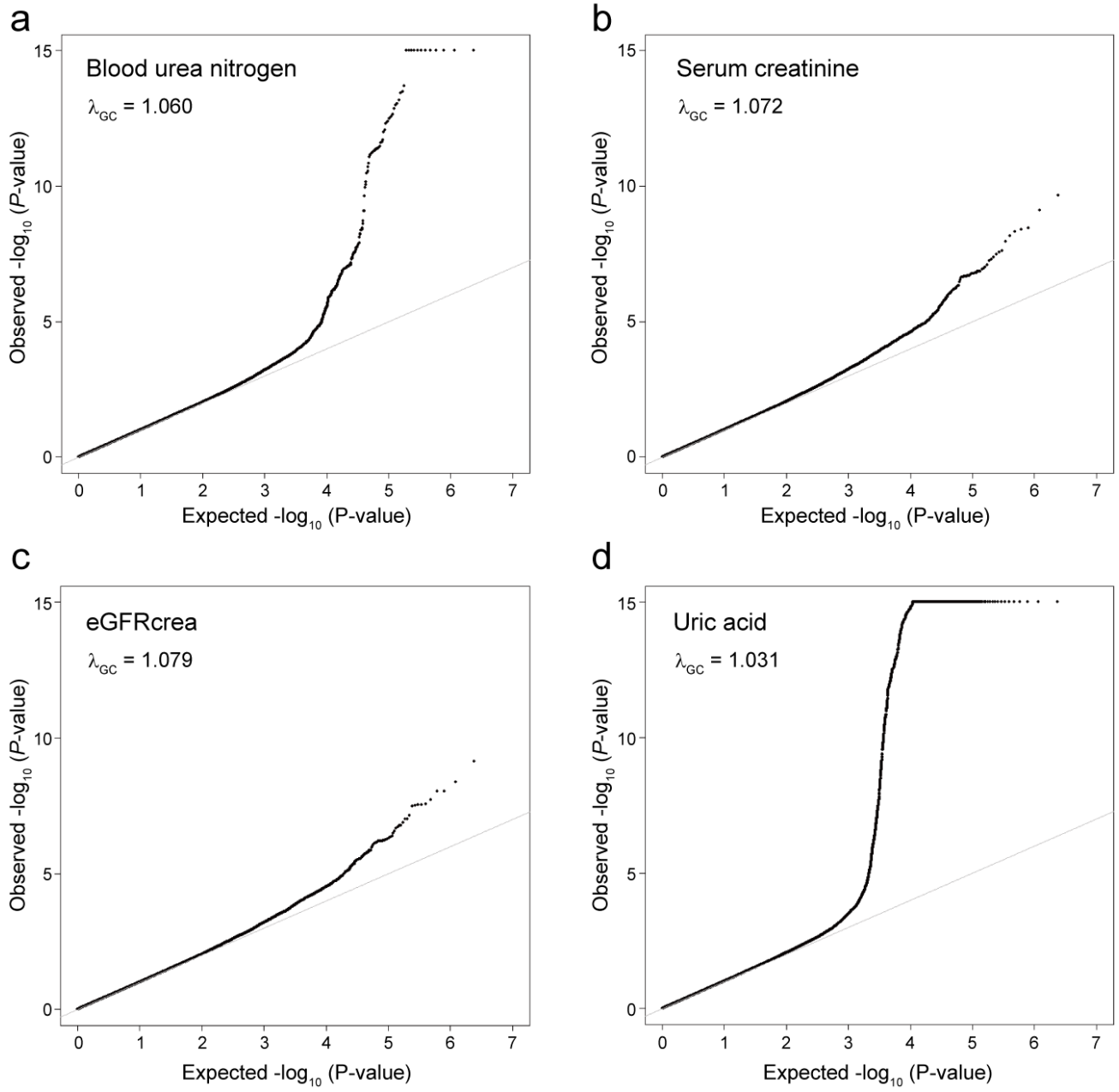
[d]*P*-value that satisfied Bonferroni's correction based on number of the loci ($\alpha = 0.05$, $n = 21$, $P < 0.0024$) are indicated in bold.

OR, odds ratio; SE, standard error; 95%CI, 95% confidence interval.

Section 2. Supplementary Figures

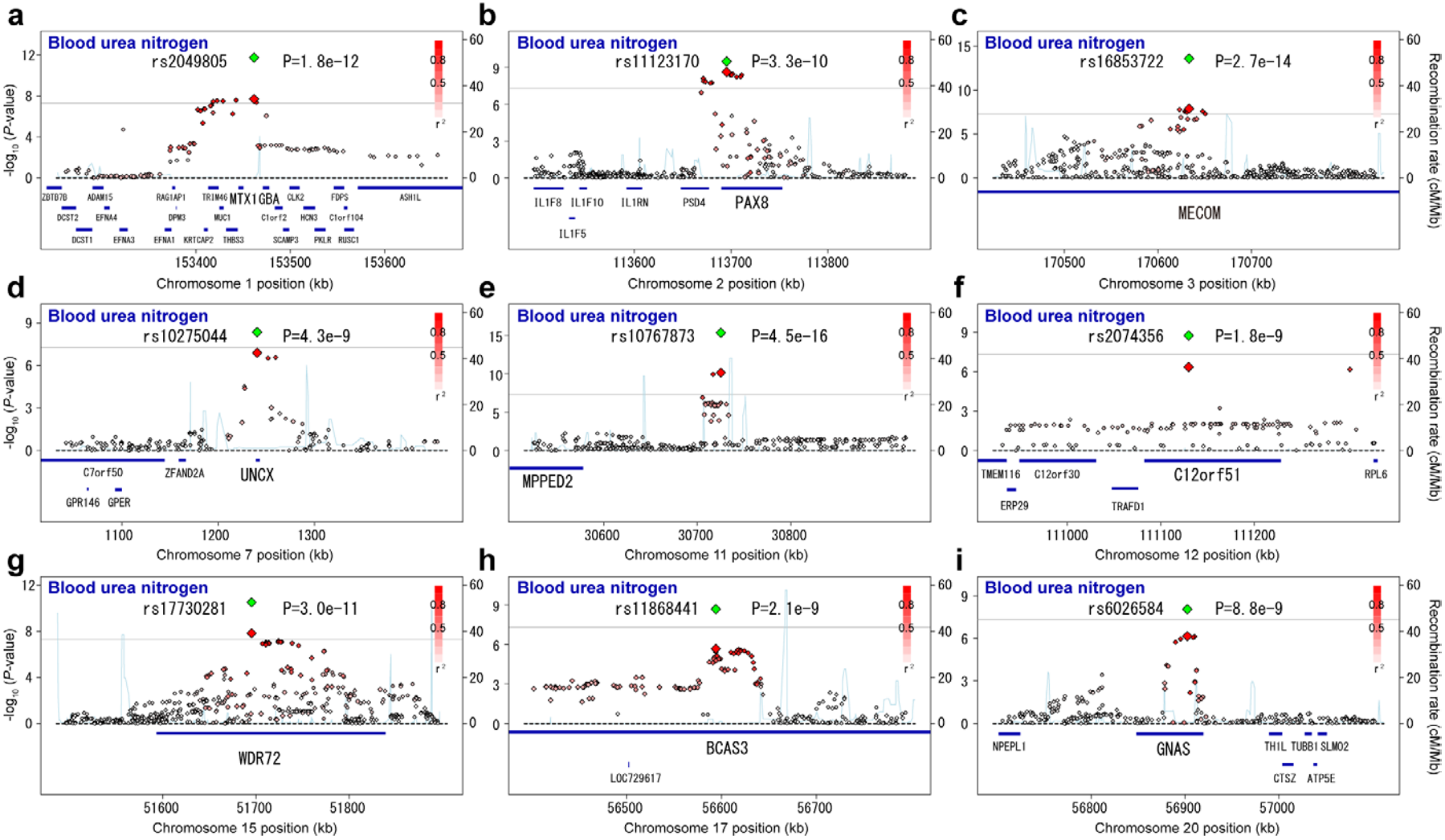
Supplementary Figure 1. Quantile-quantile plots of P-values in the GWAS meta-analysis.

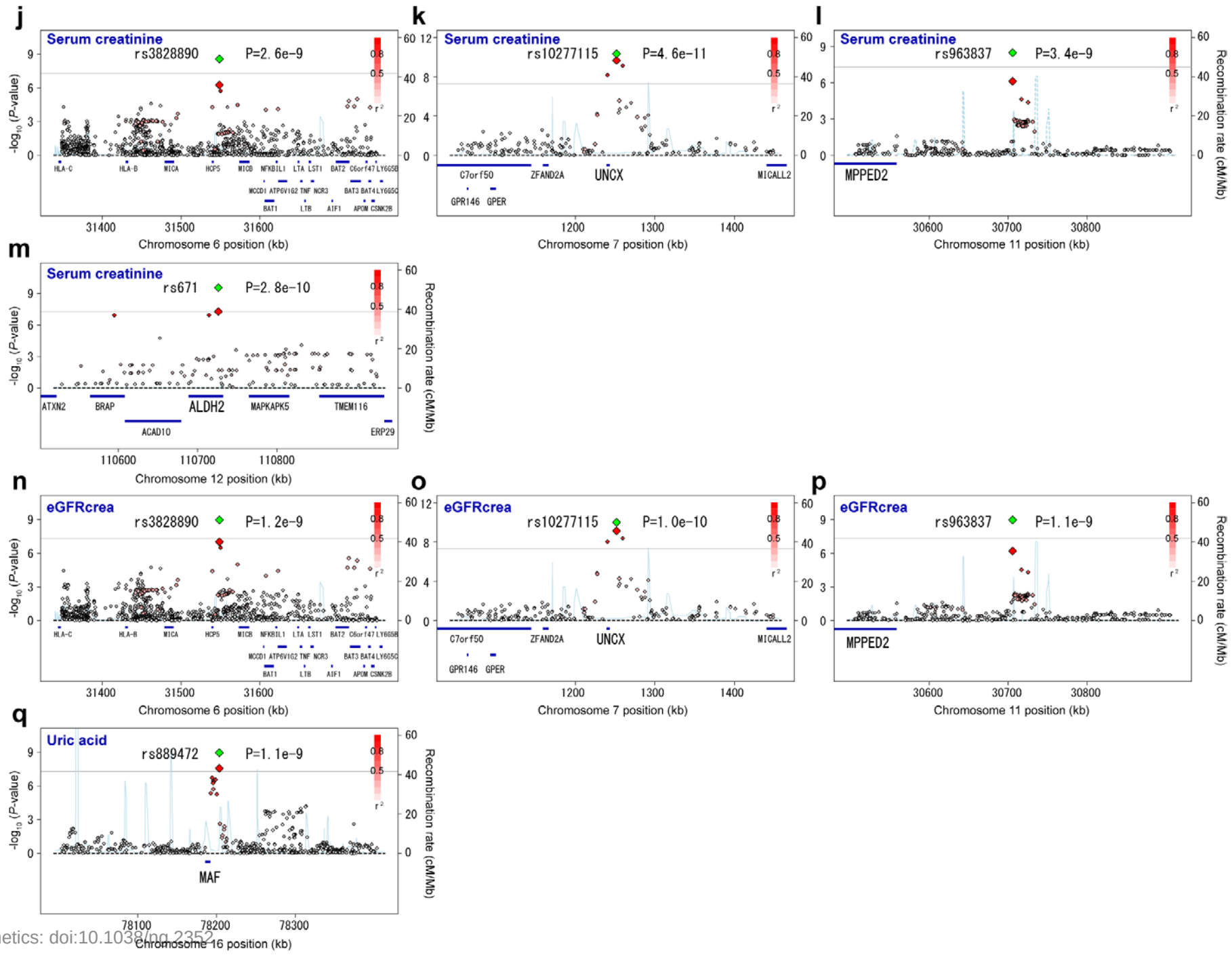
Quantile-quantile plots of *P*-values in the GWAS meta-analysis for **(a)** blood urea nitrogen, **(b)** serum creatinine, **(c)** eGFRcrea, and **(d)** uric acid. The horizontal axis indicates the expected -$\log_{10}$ (*P*-values). The vertical axis indicate the observed -$\log_{10}$ (*P*-values) after the application of genomic control correction[23,24] with inflation factor, λ_{GC}, which is indicated in each of the plots. The gray line represents $y = x$, which corresponds to the null hypothesis. The SNPs for which the *P*-values were smaller than 1.0×10^{-15} are indicated at the upper limit of the plot.



Supplementary Figure 2. Regional plots of newly identified loci associated with kidney function-related traits.

Regional plots of the SNPs in the novel loci identified for **(a-i)** blood urea nitrogen, **(j-m)** serum creatinine, **(n-p)** eGFRcrea, and **(q)** uric acid. Diamond-shaped dots represent -$\log_{10}$ (*P*-values) of the SNPs. The red diamond-shaped dots represent -$\log_{10}$ (*P*-values) of the SNPs in the GWAS meta-analysis. The density of the red color in the smaller-sized dots represents the r^2 value with the most significantly associated SNP of the larger-sized red dot. The green dot represents the *P*-value in the combined study. The blue line shows recombination rates given by the HapMap Phase II East Asian populations (release 22). The gray horizontal line represents the genome-wide significance threshold of $P = 5.0 \times 10^{-8}$. The lower portion indicates the RefSeq genes in the locus. The plots were drawn using SNAP version 2.2[37].





Nature Genetics: doi:10.1038/ng.2352

Section 3. Supplementary Note

I. Descriptions of the participating cohorts.

1. The BioBank Japan Project (BBJ).

Subjects. The BioBank Japan Project (http://biobankjp.org)[1] started at the Institute of Medical Science, the University of Tokyo in 2003 and have so far collected up to 300,000 cases consisting of 47 diseases in the bank. These subjects were recruited from 12 medical institutes in Japan including Osaka Medical Center for Cancer and Cardiovascular Diseases, the Cancer Institute Hospital of Japanese Foundation for Cancer Research, Juntendo University, Tokyo Metropolitan Geriatric Hospital, Nippon Medical School, Nihon University School of Medicine, Iwate Medical University, Tokushukai Hospitals, Shiga University of Medical Science, Fukujuji Hospital, National Hospital Organization Osaka National Hospital, and Iizuka Hospital.

In this study, a total of 44,433 subjects (46.5% females; mean ± SD age of 61.3 ± 13.2; *n* = 30,175 for the GWAS meta-analysis and *n* = 14,258 for the in-silico replication study) were enrolled and available with the data of blood urea nitrogen (*n* = 42,467), serum creatinine (*n* = 44,064), eGFRcrea (*n* = 44,245), and uric acid (*n* = 27,303). Subjects who were determined to be of non-Japanese origin by self-report, PCA, or our previous studies[2-4,21] were not included. All participants provided written informed consent as approved by the ethical committees of the RIKEN Yokohama Institute and the Institute of Medical Science, University of Tokyo.

Kidney function-related traits measurement. Clinical information for the samples in the BioBank Japan Project[1] is collected and updated annually from a self-reporting uniform questionnaire (for birth year, height, weight, and smoking and drinking habits) and from medical records (for laboratory data including the kidney function- related traits) by the professional medical coordinators according to a standardized manner.

Genotyping and imputation. We used the data of GWAS for 47 diseases which were performed for the BioBank Japan Project[1]. In the GWAS, genotyping was performed using the Illumina HumanHap550v3 Genotyping BeadChip, Illumina HumanHap610-Quad Genotyping BeadChip, Illumina HumanOmniExpress Genotyping BeadChip (Illumina, CA, USA), or oligonucleotide array of Perlegen Sciences (Perlegen Sciences, CA, USA). After excluding the subjects with call rates lower than 0.95~0.98, we excluded SNPs with call rates lower than 0.95~0.99, SNPs with ambiguous calls, or non-autosomal SNPs. We excluded closely related subjects by using identity-by-state (IBS). For each pair with 1st or 2nd degree of kinship, we excluded the member of the pair with lower call rates. We also excluded subjects whose ancestries were estimated to be distinct from the other subjects by using PCA performed by EIGENSTRAT version 2.0[38]. We performed PCA

Nature Genetics: doi:10.1038/ng.2352

for the genotype data of our study along with the genotype data of unrelated European (CEU), African (YRU), and East-Asian (Japanese and Han Chinese; JPT + CHB) individuals obtained from the Phase II HapMap database (release 24)[39]. Based on the PCA plot, we excluded the outliers in terms of ancestry from JPT + CHB clusters. We then excluded the SNPs with MAF < 0.01 or the SNPs with exact *P*-value of the Hardy-Weinberg equilibrium test < 1.0×10^{-6}~1.0×10^{-7}.

Genotype imputation was performed using MACH 1.0.16 in two step procedure[40]. The JPT and CHB individuals obtained from Phase II HapMap database (release 24)[39] were used as references. In the first step, recombination and error rate maps were estimated using 500 subjects randomly selected from the GWAS data. In the second step, genotype imputation of all subjects was conducted using the rate maps estimated in the first step. We excluded the imputed SNPs with MAF < 0.01 or *Rsq* values < 0.5.

Statistical analysis. Associations of the SNPs with transformed values of the kidney function-related traits were assessed by linear regression assuming additive effects of allele dosages using mach2qtl software[40]. Because the study population consisted of the disease cases, the affection status of the diseases were additionally included as the covariates in the association analysis, as previously described[3,4].

2. Singapore Prospective Study Program (SP2), Singapore Malay Eye Study (SiMES), and Singapore Indian Eye Study (SINDI).

Subjects. **SP2**: The Singapore Prospective Study Program (SP2) includes 6,968 participants from one of four the following previous cross-sectional studies: Thyroid and Heart Study 1982–1984[7], National Health Survey 1992[8], National University of Singapore Heart Study 1993–1995[9] or National Health Survey 1998[10]. All studies involved a random sample of individuals from the Singapore population, aged 24 to 95 years. Disproportionate sampling stratified by ethnicity was implemented to increase the number of minority ethnic groups (Malays and Asian Indians). Between 2003 to 2007, 10,747 participants were invited to participate by linking their unique national identification numbers with national registries, where 7,742 attended the interview and 5,157 of these attended the clinical examination[41]. A total of 5,499 Chinese, 1,405 Malays and 1,138 Asian-Indians were available at the time of the study and only the Chinese were used for this study.

SiMES: The Singapore Malay Eye Study (SiMES) is a population-based, cross-sectional study of Malay adults aged 40 – 80 years living in Singapore. Of the 4,168 eligible participants invited, 3,280 participated in the study yielding a response rate of 78.7%. Briefly, age-stratified random sampling of all Malay adults aged from 40–80 years residing in 15 residential districts in the southwestern part of Singapore was performed. Details of the study participants and methods have been published previously[11].

SINDI: The Singapore Indian Eye Study (SINDI) is a population-based, cross-sectional study of Asian Indian

adults aged 40–80+ years residing in the South-Western part of Singapore, as part of the Singapore Indian Chinese Cohort Eye Study. Age stratified random sampling was used to select 6,350 eligible participants, of which 3,400 participated in the study (75.6% response rate). Detailed methodology has been published[12].

SCES: The Singapore Chinese Eye Study (SCES) is a population-based, cross-sectional study of 3,300 Chinese adults aged ≥ 40 years. The study was conducted in the southwestern part of Singapore, using the same study protocol as the SiMES and SINDI. Using an age-stratified random sampling strategy, 6,350 names were selected. Overall, there was a participation rate of 73% among these selected Chinese who were eligible.

Informed consent and ethics committees

Informed consent was obtained for all subjects in all our studies.

SP2 was approved by the Singapore Health Services Institutional Review Board (ref CIRB 2001/001/C). Genetic analysis was approved under the National Health Care Group Domain Specific Review Board (C/09/413).

SiMES was approved by Singapore Eye Research Institute Scientific & Ethics Committee (R341/34/2003). Collection of blood and urine sample for blood chemistry, genetic association and renal function studies was also approved by Singapore Eye Research Institute Scientific & Ethics Committee (R382/40/2004)

SINDI and SCES were approved by Singapore Health Services Institutional Review Board (ref CIRB 2006/612/A) under the study title of Singapore Eye Disease Study (SEDS) - The Indian / Chinese Cohort (SICC).

Kidney function-related traits. **SP2**: Creatinine was measured from non-fasting venous samples using enzymatic methods implemented in the Advia 2400 Chemistry System (Siemens Medical Solutions Diagnostics, Deerfield, IL, USA) at the National University Hospital Referral Laboratory. The new National Institute of Standards and Technology Standard Reference Material (NIST SRM) 967, Creatinine in Frozen Human Serum, was developed in collaboration with the National Kidney Disease Education Program and the College of American Pathologists for improved calibration of clinical instruments and procedures for measuring serum creatinine.

SiMES: A 40-mL sample of non-fasting venous blood was collected to determine levels of serum lipids (total cholesterol, HDL cholesterol, direct LDL cholesterol), glycosylated hemoglobin A_{1C} (HbA_{1C}), creatinine, and casual glucose at the National University Hospital Reference Laboratory for measurement on the same day[11]. Serum creatinine was measured using the same protocol as SP2 in the same laboratory.

SINDI and SCES: Non fasting venous blood sample was collected for biochemistry tests including serum lipids,

HbA_{1C}, creatinine and random glucose. The creatinine analysis is performed on the DXC (Beckman Coulter), using the Jaffe method.

Genotyping. **SP2**: 2,867 blood derived samples from the Chinese SP2 study were genotyped on a combination of Illumina HumanHap 610Quad, 1Mduov3 and 550v3 Beadchips. The samples on the 610Quad and 1M arrays were controls for a Type 2 Diabetes study and quality filters were implemented on a case-control basis. Details of the quality controls have been described elsewhere[42].
SiMES: For the Malay SiMES study, 3,072 samples were genotyped on the Illumina HumanHap 610Quad.
SINDI: For the SINDI study, 2,953 samples were genotyped on the Illumina HumanHap 610Quad.
SCES: 1,949 blood samples were genotyped on the Illumina HumanHap 610Quad.

For each array in each cohort, a first round of clustering was performed with the proprietary clustering files from Illumina on the Beadstudio using GenCall. Samples achieving a 99% call rate were used to generate local specific clusterfiles (GenTrain) which were used for a final round of genotype calling. A threshold of 0.15 was implemented on the GenCall score to decide on the confidence of the assigned genotypes.

Quality control. Similar quality control procedures were implemented on each cohort. SNP QC was first performed to obtain a pseudo-cleaned set of genotypes for sample QC. SNPs that had missingness greater than 5%, gross departure from HWE (P-value < 1.0×10^{-6}) or minor allele frequency equal to zero were temporarily removed from the data.

Using the pseudo-clean set of genotype, samples were then removed based on the following conditions and in the following order: (i) sample missingness (samples will have a minimum call rate of 95%); (ii) excessive heterozygosity; (iii) cryptic relatedness; (iv) discordant ethnic membership, using principal components analysis[38] (PCA) with 4 panels from International HapMap II and the Singapore Genome Variation Project[43] which includes 96 Chinese, 89 Malays and 83 Asian Indians from Singapore; (v) gender discrepancy.

Finally, after removing the problematic samples and with the full set of SNPs on the genotyping array, SNP QC is repeated, removing SNPs that had missingness greater than 5%, gross departure from HWE (P-value < 10^{-4} for the Chinese and P-value < 10^{-6} for the Malays and Indians) or minor allele frequency equal to zero across the samples. After QC, there are 2,434 SP2, 2,542 SiMES, 2,538 SINDI, and 1,889 SCES samples available with genotypes. The post-QC SNPs were used for imputation against reference panels and association analysis.

Imputation. Imputation was performed using IMPUTEv0.5.0[44] (for SP2, SiMES and SINDI) and IMPUTEv2[45] (for SCES). For SP2 Chinese, the reference panel is build 36, release 22 db126 JPT+CHB HapMap panel of

2,416,663 SNPs. For the SiMES Malays and SINDI Indians, a combined panel of the HapMap Phase II panels (build 36, release 22 db126 CEU and JPT+CHB and YRI HapMap panel of 1969737 SNPs) was used for the imputation.

Statistical analysis. SNPTESTv2.1.1 (SP2, SiMES and SINDI) and SNPTESTv2.2 (SCES) were used to perform the association tests, using the –methods score option. The imputation_quality here is the score_info generated by SNPTEST for the association tests. SNPs with imputation quality score less than 0.5 were excluded from meta-analysis.

3. Korea Association Resource project (KARE).

Subjects. The Korea Association Resource (KARE) study was initiated in 2007 to undertake a large-scale GWA analysis for Type 2 Diabetes and numerous complex quantitative traits amongst the 10,038 participants (aged between 40 and 69) of the Ansung (n = 5,018) and Ansan (n = 5,020) population-based cohorts. Two KARE study cohorts were established as part of the Korean Genome Epidemiology Study (KoGES) in 2001. The sampling base for both cohorts is in KyungGi-Do province, close to Seoul, the capital of the Republic of Korea. A total of 8,842 subjects (52.7% females; mean ± SD age of 52.2 ± 89) were available with the data of blood urea nitrogen (BUN). Written informed consent for cohort examinations approved by Research Ethics Committees was obtained from all cohort participants.

Kidney function-related traits. Both KARE cohorts were designed to allow longitudinal prospective study and adopted the same investigational strategy. Participants have been examined every two years since baseline (2001). More than 260 traits have been extensively examined through epidemiological surveys, physical examinations, and laboratory tests applied to Ansung and Ansan cohort members[6,13,14]. Blood urea nitrogen was measured using urease with coupled enzymes.

Genotyping and imputation. About 10,000 subjects from KARE study cohorts were genotyped with Affymetrix Genome-Wide Human SNP array 5.0. We excluded samples with genotyping call rate < 0.98, gender inconsistency, heterozygosity and first-degree cryptic relationships. After sample quality control, we excluded SNPs with call rates lower than 0.95, minor allele frequency lower than 0.01 and Hardy-Weinberg violation (HWE P-value < 1.0×10^{-6}). Genotype imputation was performed using IMPUTE program. Genotype information for HapMap Asian (JPT + CHB) population was used as reference panel based on release 22 / NCBI build 36 and dbSNP bulid 128 for SNP imputation. We excluded the imputed SNPs with low genotype information content (< 0.5), posterior probability score < 0.90, call rate < 0.90, MAF < 0.01, and

HWE *P*-value < 1.0×10^{-7} [6,13,14].

Statistical analysis. The genetic associations of Kidney function-related traits were tested by linear regression analysis with additive genetic mode using PLINK program. Association analyses for $\log_{10}$(BUN) was adjusted with age, gender, recruitment area and BMI.

4. Health Examinee shared control study (HEXA).

Subjects. The HEXA cohort is one of the KoGES population-based cohorts which were initiated in 2001 aiming to identify risk factors of life-style related complex diseases such as type 2 diabetes, hypertension, and dyslipidemia. Approximately 3,700 of 1,200,000 subjects aged 40-69 from the HEXA cohort were randomly selected as a shared control group for the Korean cancer and coronary artery disease (CAD) GWA studies. Genotyping was conducted with the Affymetrix Genome-Wide Human SNP array 6.0 in 2008. Written informed consent for cohort examinations approved by Research Ethics Committees was obtained from all cohort participants.

Kidney function-related traits. Kidney functions were measured from fasting subjects by clinical examinations. Kidney function-related traits such blood urea nitrogen, serum creatinine, and uric acid were assayed using the enzymatic reaction.

Genotyping and imputation. HEXA was conducted using Affymetrix Genome-Wide Human SNP array 6.0. We included unrelated samples with missing genotyping call rate below 2% and excluded the samples with gender inconsistency or heterozygosity. After sample quality control, we included SNPs with call rates lower below 5%, minor allele frequency upper than 0.99 and Hardy-Weinberg (HWE *P*-value > 1.0×10^{-6}). Genotype imputation was performed using IMPUTE program reference panel base HapMap Asian (JTP + CHB) population on release 22 / NCBI build 36 and dbSNP bulid 128. We included the imputed SNPs with high genotype information content (> 0.5), posterior probability score > 0.90, call rate > 0.90, MAF > 0.01, and HWE *P*-value > 1.0×10^{-7} [14].

Statistical analysis. Measuring kidney functions, the value of genetic associations were tested by linear regression analysis assuming additive effect using PLINK program. Age, gender, recruitment area and BMI as additional covariates were included in the association analysis.

5. Taiwan Super Control Study (TWSC)[15] and Taiwan Type 2 Diabetes Consortium (TWT2D)[16].

Subjects. In this study, 986 control samples (49.8% females; mean ± SD age of 50.7 ± 17.4) were randomly selected from the Taiwan Han Chinese Cell and Genome Bank, a more than 3,300 healthy controls database, which was recruited via stratified, 3-staged, probability clustering sampling scheme throughout the registry of all the 329 non-aboriginal townships or city districts in Taiwan from 2002 to 2004[6]. The criteria for controls in the association were (1) no past diagnostic history of T2D, (2) HbA_{1C} ranging from 3.4 to 6.0, and (3) BMI ≤ 32. The two control groups were comparable with respect to BMI, gender, age at study, and level of HbA_{1C}. A total of 987 unrelated individuals with T2D and age > 20 years (50.0% females; mean ± SD age of 59.2 ± 10.2) were recruited from China Medical University Hospital (CMUH), Taichung. All of the T2D cases were diagnosed according to medical records and fasting plasma glucose levels using American Diabetic Association Criteria. Subjects with type 1 diabetes, gestational diabetes, and maturity-onset diabetes of the young (MODY) were excluded from this study. All of the participating T2D cases and controls were of Han Chinese origin, which is the origin of 98% of the Taiwan population[17]. The study was approved by the institutional review board of all the participating hospitals and Academia Sinica, Taiwan, and written informed consent were obtained from all of the participants.

Kidney function-related traits. Phenotype questionnaire on ethnicity, disease history and medication, life styles, and cognitive function of the elderly was administered by well-trained nurses in a door-to-door survey, following a standardized protocol. Clinical measurements including basic blood chemistry, and anthropometric parameters were obtained from Taiwan Han Chinese Cell and Genome Bank blood sample.

Genotyping and imputation. In GWAS, genotyping was conducted using the Illumina HumanHap550-Duo BeadChip (Illumina, San Diego, CA, USA) and performed by deCODE genetics (Reykjavík, Iceland). Genotype calling was determined by Beadstudio (Illumina) using default parameters. After filtering callrate < 0.95, MAF < 0.01, HWE-P < 1.0×10^{-6} SNPs, imputation was performed using IMPUTE v2 software to generate imputed genotype data, HapMap Phase II JPT_CHB_r24_nr.b36_fwd genotype data was used as reference panel to IMPUTE.

Statistical analysis. Associations of the SNPs with transformed values of the kidney function-related traits were assessed by linear regression assuming additive effects of allele dosages using SNPTEST v2 software. Sex, age, smoking, and drinking status were included as covariates in the linear regression models. The analyses for SC and T2D were performed separately due to the difference between the two samples.

6. The Genetic Epidemiology Network of Salt-Sensitivity (GenSalt) study

Subjects. The GenSalt study is a unique NHLBI-sponsored family feeding-study designed to examine the interaction between genes and dietary sodium and potassium intake on blood pressure (BP). A detailed description of the GenSalt study design and participants has been reported previously[18]. Briefly, 3,142 participants from 633 Han families from rural, north China were ascertained through a proband with untreated systolic BP 130-160 mmHg or diastolic BP 85-100 mmHg from a population-based BP screening. A total of 1,906 GenSalt probands and their siblings, spouses, and offspring took part in the dietary intervention and GWA study. Written informed consent for cohort examinations approved by Research Ethics Committees was obtained from all the participants in the study.

Kidney function-related traits. Overnight fasting blood specimens were collected at baseline examination for measurement of serum creatinine. Blood specimens were processed at each field center and shipped by air to the central clinical laboratory at the at Fuwai Hospital of the Chinese Academy of Medical Sciences in Beijing, where the specimens were stored at −70°C until laboratory assays could be performed. Serum creatinine was measured by the modified kinetic Jaffe reaction on a Hitachi 7060 Clinical Analyzer (Hitachi High-Technologies Corporation, Tokyo, Japan) using commercial reagents. In addition, a random sample of 60 serum specimens was sent to the Cleveland Clinic Laboratory (Cleveland, OH, USA) for measurement of serum creatinine where the Modification of Diet in Renal Disease (MDRD) Study measured serum creatinine levels. On average, serum creatinine assays on the same samples were 0.0338 mg/dL higher in the Cleveland Clinic Laboratory than in the InterASIA Study laboratory. Therefore, serum creatinine measurements among study participants were calibrated by adding this difference to calculated estimated glomerular filtration rate (eGFR) using the simplified MDRD equation[46].

Genotyping and imputation. Lymphocytic DNA samples were obtained from GenSalt family members (probands, parents, spouses, siblings, and offspring). Genome-wide SNPs were genotyped using Affymetrix® Genome-Wide Human Array 6.0 at the Affymetrix genotyping facility. After removing sex-linked SNPs, mitochondrial SNPs, and 'unassigned' SNPs that had no annotated chromosomal location, 871,166 SNPs were chosen for examination. Strict procedures for extensive QC were used to check the data for any obvious errors, remove uninformative data, and find and remove all Mendelian errors in three stages. In stage 1, we removed subjects with gender discrepancies between reported sex and that estimated by PLINK[47] and those who had potential pedigree errors, as determined by GRR (graphical representation of relationship errors)[48]. In stage 2, we removed monomorphic SNPs, Affymetrix 'housekeeping' SNPs, SNPs with missing rates of > 0.25 or MAF of < 0.01. In the final stage, Mendelian errors were found and removed using PLINK[47] and PedCheck[49]. After the QC process, 820,015 autosomal SNPs from 1,881 subjects remained. An additional

1,792,556 SNPs were imputed from a HapMap reference panel using 90 subjects from the JPT and CHB populations. The QC processes removed imputed SNPs with $R^2 < 0.5$, MAF < 0.01, Hardy-Weinberg *P*-value $< 1.0 \times 10^{-6}$, Mendelian errors.

Statistical analysis. Analyses of the association between SNPs and serum creatinine or eGFR phenotypes were conducted using a linear mixed-effects model implemented in the Proc Mixed procedure of SAS (version 9.1; SAS Institute, Cary, NC). A "sandwich" option was used to compute the estimated variance-covariance matrix of the fixed-effects (genetic variant effects) parameters by using the asymptotically consistent estimator. Because most of the studied families (random effects) only included sib pairs, we selected compound symmetry as the covariance structure, which assumes the same degree of dependency among family members. Additive genetic models were assumed.

7. Cardio-metabolic Genome Epidemiology (CAGE).

Subjects. The Cardio-metabolic Genome Epidemiology (CAGE) Network is an ongoing collaborative effort to investigate genetic and environmental factors and their interactions affecting cardiometabolic traits/disorders among Asians, including the Japanese[19,20]. CAGE participants were recruited in a population-based or hospital-based setting, depending on the design of the member studies. Participation rates varied among the member studies (approximately from 25% in the community-based survey to 80% in the work place-based survey). From this network sample, a total of 988 Japanese samples (576 men and 412 women; age range 36–85, median 64 years) were used for a GWAS of kidney function-related traits, such as serum creatinine level. These participants were enrolled at two separate sites in Japan, the Tokyo and Osaka districts. In the CAGE Network, all participants provided written informed consent and studies were approved by local Research Ethics Committees and/or Institutional Review boards.

Kidney function-related traits. Serum creatinine was measured using a modified kinetic Jaffe reaction in all member studies. eGFRcrea was calculated using the equation recommended by the Japanese Society of Nephrology (http://www.jsn.or.jp/en/). Clinical information for the participants in the CAGE Network is collected from a self-reporting questionnaire (for birth year, smoking and drinking habits) and from medical (or annual health check-up) records (for laboratory data including the kidney function-related traits) by the trained personnel. Participants' height and body weight were also measured by trained personnel using standard anthropometric techniques.

Genotyping and imputation. Genotyping was performed with Infinium HumanHap550/Human610-Quad

BeadArray (Illumina, San Diego, CA, USA), which interrogated 550K/610K SNPs, according to the manufacturer's protocol. This set of SNP markers reportedly captures 87% of common SNPs with an LD coefficient of $r^2 > 0.8$ in the HapMap JPT and CHB populations (according to the manufacturer's brochure). Assay accuracy and reproducibility were measured by using DNA from CEU samples genotyped as part of the HapMap project [http://www.hapmap.org]. Genotype calling was performed using BeadStudio software (Illumina) and genotype calls with a 'GenCall' Score < 0.53 were dropped from the analysis. The GenCall Score measures the reliability of genotype calls based on the clustering of dye intensities (www.illumina.com/downloads/ GenCallTechSpotlight.pdf).

QC of SNPs and samples was performed as previously described[20]. Briefly, data cleaning and analysis were performed using PLINK software (version 1.06)[47]. Among the assayed SNPs, we excluded SNPs for the following: (i) genotype call rate < 0.95; (ii) significant ($P < 1.0 \times 10^{-6}$) deviation from HWE; or (iii) MAF < 0.01. The remaining 451,377 SNPs were analyzed in the genome scan.

We used BEAGLE (ver 3.0.4)[50] for imputation. The training set comprised genotypes for HapMap Asians (45 JPT + 45 CHB; Phase 2, Release 24). We imputed uncalled genotypes for assayed SNPs, resulting in 100% genotypes called for all SNPs, whether assayed or not.

Statistical analysis. Association testing was done using PLINK (ver 1.06) and the *R* software (ver 2.12.2).

II. Contributing authors participating in the KidneyGen, CKDGen, and GUGC consortia

II-a : Contributing authors in the KidneyGen consortium.

John C Chambers[1,2], Weihua Zhang[1,2], Graham M Lord[3–5], Pim van der Harst[6], Debbie A Lawlor[7], Joban S Sehmi[2,8], Daniel P Gale[9], Mark N Wass[10], Kourosh R Ahmadi[11], Stephan J L Bakker[6], Jacqui Beckmann[12], Henk J G Bilo[6], Murielle Bochud[13], Morris J Brown[14], Mark J Caulfield[15], John M C Connell[16], H Terence Cook[17], Ioana Cotlarciuc[11], George Davey Smith[7], Ranil de Silva[2,8], Guohong Deng[18], Olivier Devuyst[19], Lambert D Dikkeschei[20], Nada Dimkovic[21], Mark Dockrell[22], Anna Dominiczak[16], Shah Ebrahim[23], Thomas Eggermann[24], Martin Farrall[25], Luigi Ferrucci[26], Jurgen Floege[27], Nita G Forouhi[28], Ron T Gansevoort[29], Xijin Han[30], Bo Hedblad[31], Jaap J Homan van der Heide[32], Bouke G Hepkema[33], Maria Hernandez-Fuentes[3–5], Elina Hypponen[34], Toby Johnson[35], Paul E de Jong[36], Nanne Kleefstra[36], Vasiliki Lagou[37], Marta Lapsley[22], Yun Li[30], Ruth J F Loos[28], Jian'an Luan[28], Karin Luttropp[38], Céline Maréchal[19], Olle Melander[31], Patricia B Munroe[15], Louise Nordfors[38], Afshin Parsa[39], Leena Peltonen[40–42], Brenda W Penninx[43–45], Esperanza Perucha[3–5], Anneli Pouta[42,46], Inga Prokopenko[47–49], Paul J Roderick[50], Aimo Ruokonen[51], Nilesh J Samani[52], Serena Sanna[53], Martin Schalling[54], David Schlessinger[55], Georg Schlieper[27], Marc A J Seelen[29], Alan R Shuldiner[56], Marketa Sjögren[31], Johannes H Smit[43–45], Harold Snieder[37], Nicole Soranzo[11], Timothy D Spector[11], Peter Stenvinkel[57], Michael J E Sternberg[10], Ramasamyiyer Swaminathan[58], Toshiko Tanaka[26], Lielith J Ubink-Veltmaat[59], Manuela Uda[53], Peter Vollenweider[60], Chris Wallace[61], Dawn Waterworth[62], Klaus Zerres[24], Gerard Waeber[60], Nicholas J Wareham[28], Patrick H Maxwell[9], Mark I McCarthy[47–49], Marjo-Riitta Jarvelin[1,42,46,63], Vincent Mooser[62], Goncalo R Abecasis[30], Liz Lightstone[64], James Scott[8], Gerjan Navis[6], Paul Elliott[1,65] & Jaspal S Kooner[2,8].

1. Department of Epidemiology and Biostatistics, School of Public Health, Imperial College of London, London, UK.
2. Ealing Hospital National Health Service (NHS) Trust, Middlesex, UK.
3. Department of Nephrology and Transplantation and 4. Medical Research Council (MRC) Centre for Transplantation, King's College London, UK.
5. National Institute for Health Research (NIHR) Comprehensive Biomedical Research Centre, Guy's and St. Thomas' NHS Foundation Trust and King's College London, London, UK.
6. University Medical Center Groningen, University of Groningen, Groningen, The Netherlands.
7. MRC Centre for Causal Analyses in Translational Epidemiology, University of Bristol, Bristol, UK.
8. National Heart and Lung Institute, Hammersmith Hospital Campus, Imperial College London, London, UK.
9. Division of Medicine, University College London, London, UK.

10. Structural Bioinformatics Group, Imperial College London, London, UK.
11. Twin Research and Genetic Epidemiology Department, King's College London, St. Thomas' Hospital Campus, London, UK.
12. Department of Medical Genetics, University of Lausanne, Lausanne, Switzerland.
13. University Institute of Social and Preventive Medicine, Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland.
14. Clinical Pharmacology Unit, University of Cambridge, Addenbrookes Hospital, Cambridge, UK.
15. Clinical Pharmacology and The Genome Centre, William Harvey Research Institute, Barts and The London School of Medicine and Dentistry, London, UK.
16. Glasgow Cardiovascular Research Centre, University of Glasgow, Glasgow, UK.
17. Department of Histopathology, Imperial College, Hammersmith Hospital, London, UK.
18. Department of Gastroenterology and Hepatology, Imperial College London, London, UK.
19. Division of Nephrology, Université Catholique de Louvain Medical School, Brussels, Belgium.
20. Isala Clinics, Zwolle, The Netherlands.
21. Center for Renal Diseases, Zvezdara University Medical Center, Belgrade, Serbia.
22. South West Thames Institute for Renal Research, Epsom and St. Helier University Hospitals NHS Trust, Carshalton, UK.
23. London School of Hygiene and Tropical Medicine, London, UK.
24. Department of Human Genetics, Rheinisch-Westfaelische Technische Hochschule University Hospital Aachen, Aachen, Germany.
25. Cardiovascular Medicine, University of Oxford, Wellcome Trust Centre for Human Genetics, Oxford, UK.
26. National Institute of Aging, Clinical Research Branch–Longitudinal Studies Section, Baltimore, Maryland, USA.
27. Department of Nephrology and Clinical Immunology, RWTH University Hospital Aachen, Aachen, Germany.
28. MRC Epidemiology Unit, Institute of Metabolic Science, Addenbrooke's Hospital, Cambridge, UK.
29. Department of Internal Medicine, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands.
30. Center for Statistical Genetics, University of Michigan, Ann Arbor, Michigan, USA.
31. Department of Clinical Sciences, Lund University, Malmö, Sweden.
32. Department of Nephrology, University Medical Center Groningen, Groningen, The Netherlands.
33. Department of Transplantation Immunology, University Medical Center Groningen, Groningen, The Netherlands.
34. Centre of Epidemiology for Child Health, University College London Institute of Child Health, London, UK.

35. Department of Medical Genetics, University of Lausanne and the Swiss Institute of Bioinformatics, Lausanne, Switzerland.
36. Langerhans Medical Research Group, Zwolle, The Netherlands.
37. Unit of Genetic Epidemiology and Bioinformatics, Department of Epidemiology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands.
38. Department of Molecular Medicine and Surgery, Karolinska University Hospital, Karolinska Institutet, Stockholm, Sweden.
39. Division of Nephrology, University of Maryland School of Medicine, Baltimore, Maryland, USA.
40. Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Hinxton, Cambridge, UK.
41. Institute for Molecular Medicine Finland (FIMM), Nordic European Molecular Biology Laboratory (EMBL) Partnership for Molecular Medicine, Biomedicum Helsinki 2U and University of Helsinki, Helsinki, Finland.
42. National Institute for Health and Welfare, Helsinki, Finland.
43. Department of Psychiatry, Institute for Research in Extramural Medicine (EMGO), Neuroscience Campus, Vrije Universiteit (VU) Medical Center, Amsterdam, The Netherlands.
44. Department of Psychiatry, Leiden University Medical Center, Leiden, The Netherlands.
45. Department of Psychiatry, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands.
46. Institute of Health Sciences, University of Oulu, Oulu, Finland.
47. Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford, UK.
48. Oxford Centre for Diabetes, Endocrinology and Metabolism and 49. Oxford NIHR Biomedical Research Centre, Oxford, UK.
50. University of Southampton, Southampton, UK.
51. Institute of Clinical Medicine, Department of Clinical Chemistry, University of Oulu, Oulu, Finland.
52. Cardiovascular Sciences, University of Leicester, Glenfield Hospital, Leicester, UK.
53. Istituto di Neurogenetica e Neurofarmacologia, Consiglio Nazionale delle Ricerche, Cagliari, Italy.
54. Department of Molecular Medicine and Surgery, Karolinska University Hospital, Karolinska Institutet, Stockholm, Sweden.
55. Laboratory of Genetics, US National Institutes of Health Biomedical Research Center, National Institute on Aging, Baltimore, Maryland, USA.
56. Division of Endocrinology, Diabetes and Nutrition, University of Maryland School of Medicine, Baltimore, Maryland, USA.
57. Division of Renal Medicine K56, Karolinska University Hospital at Huddinge, Stockholm, Sweden.
58. Chemical Pathology, Guy's and St Thomas' Hospitals Trust, London, UK.

59. General Practice ‘t Veen, Hattem, The Netherlands.
60. Department of Internal Medicine, University Hospital Center, University of Lausanne, Lausanne, Switzerland.
61. Cambridge Institute for Medical Research, Addenbrooke’s Hospital, Hills Road, Cambridge, UK.
62. Medical Genetics, Clinical Pharmacology and Discovery Medicine, GlaxoSmithKline, King of Prussia, Pennsylvania, USA.
63. Biocenter Oulu, University of Oulu, Oulu, Finland.
64. Renal Section, Division of Medicine, Hammersmith Hospital Campus, Imperial College London, London, UK.
65. MRC-HPA Centre for Environment and Health, Department of Epidemiology and Biostatistics, School of Public Health, Imperial College of London, London, UK.

II-b : Contributing authors in the CKDGen consortium.

Anna Köttgen[1,2], Cristian Pattaro[3,4], Carsten A Böger[5], Christian Fuchsberger[3,4], Matthias Olden[5,6], Nicole L Glazer[7,8], Afshin Parsa[9], Xiaoyi Gao[10], Qiong Yang[11], Albert V Smith[12,13], Jeffrey R O’Connell[9], Man Li[1], Helena Schmidt[14], Toshiko Tanaka[15,16], Aaron Isaacs[17], Shamika Ketkar[10], Shih-Jen Hwang[18,19], Andrew D Johnson[18,19], Abbas Dehghan[17,20], Alexander Teumer[21], Guillaume Paré[22], Elizabeth J Atkinson[23], Tanja Zeller[24], Kurt Lohman[25], Marilyn C Cornelis[26], Nicole M Probst-Hensch[27,28], Florian Kronenberg[29], Anke Tönjes[30], Caroline Hayward[31], Thor Aspelund[12,13], Gudny Eiriksdottir[12], Lenore J Launer[32], Tamara B Harris[32], Evadnie Rampersaud[33], Braxton D Mitchell[9], Dan E Arking[34], Eric Boerwinkle[35], Maksim Struchalin[36], Margherita Cavalieri[37], Andrew Singleton[38], Francesco Giallauria[39], Jeffrey Metter[39], Ian H de Boer[40], Talin Haritunians[41], Thomas Lumley[42], David Siscovick[8,43], Bruce M Psaty[44–46], M Carola Zillikens[20,47], Ben A Oostra[17], Mary Feitosa[10], Michael Province[10], Mariza de Andrade[23], Stephen T Turner[48], Arne Schillert[49], Andreas Ziegler[49], Philipp S Wild[24], Renate B Schnabel[24], Sandra Wilde[24], Thomas F Munzel[24], Tennille S Leak[50], Thomas Illig[51], Norman Klopp[51], Christa Meisinger[51], H-Erich Wichmann[51–53], Wolfgang Koenig[54], Lina Zgaga[55], Tatijana Zemunik[56], Ivana Kolcic[57], Cosetta Minelli[3,4], Frank B Hu[26], Åsa Johansson[58], Wilmar Igl[58], Ghazal Zaboli[58], Sarah H Wild[55], Alan F Wright[31], Harry Campbell[55], David Ellinghaus[59], Stefan Schreiber[59], Yurii S Aulchenko[17,20], Janine F Felix[17,20], Fernando Rivadeneira[17,20,47], Andre G Uitterlinden[17,20,47], Albert Hofman[17,20], Medea Imboden[27,28], Dorothea Nitsch[60], Anita Brandstätter[29], Barbara Kollerits[29], Lyudmyla Kedenko[61], Reedik Mägi[62,63], Michael Stumvoll[30], Peter Kovacs[30], Mladen Boban[56], Susan Campbell[31], Karlhans Endlich[64], Henry Völzke[65], Heyo K Kroemer[66], Matthias Nauck[67], Uwe Völker[21], Ozren Polasek[57], Veronique Vitart[31], Sunita Badola[68], Alexander N Parker[68], Paul M Ridker[69], Sharon L R Kardia[70], Stefan Blankenberg[24], Yongmei Liu[71],

Gary C Curhan[72], Andre Franke[59], Thierry Rochat7[3], Bernhard Paulweber[61], Inga Prokopenko[62,63], Wei Wang[56,74], Vilmundur Gudnason[12,13], Alan R Shuldiner[9], Josef Coresh[1,75], Reinhold Schmidt[37], Luigi Ferrucci[39], Michael G Shlipak[76], Cornelia M van Duijn[17,20], Ingrid Borecki[10], Bernhard K Krämer[77], Igor Rudan[55], Ulf Gyllensten[58], James F Wilson[55], Jacqueline C Witteman[17,20], Peter P Pramstaller[3,4], Rainer Rettig[78], Nick Hastie[31], Daniel I Chasman[69], W H Kao[1,75], Iris M Heid[6,51] & Caroline S Fox[18,19,79].

1. Department of Epidemiology, Johns Hopkins University, Baltimore, Maryland, USA.
2. Renal Division, University Hospital of Freiburg, Freiburg, Germany.
3. Institute of Genetic Medicine, European Academy Bozen/Bolzano (EURAC), Bolzano, Italy.
4. Affiliated Institute of the University of Lübeck, Germany, Viale Druso, Bolzano, Italy.
5. Department of Internal Medicine II, University Medical Center Regensburg, Regensburg, Germany.
6. Department of Epidemiology and Preventive Medicine, University Medical Center Regensburg, Regensburg, Germany.
7. Cardiovascular Health Research Unit, University of Washington, Seattle, Washington, USA.
8. Department of Medicine, University of Washington, Seattle, Washington, USA.
9. University of Maryland Medical School, Baltimore, Maryland, USA.
10. Division of Statistical Genomics, Washington University School of Medicine, St. Louis, Missouri, USA.
11. Department of Biostatistics, Boston University School of Public Health, Boston, Massachusetts, USA.
12. Icelandic Heart Association, Kopavogur, Iceland.
13. University of Iceland, Reykjavik, Iceland.
14. Department of Neurogeriatrics, Austrian Stroke Prevention Study, Institute of Molecular Biology and Biochemistry and University Clinic of Neurology, Medical University Graz, Graz, Austria.
15. Clinical Research Branch, National Institute on Aging, Baltimore, Maryland, USA.
16. Medstar Research Institute, Baltimore, Maryland, USA.
17. Department of Epidemiology, Erasmus MC, Rotterdam, The Netherlands.
18. The National Heart, Lung, and Blood Institute's Framingham Heart Study, Framingham, Massachusetts, USA.
19. Center for Population Studies, Framingham, Massachusetts, USA.
20. Netherlands Genomics Initiative (NGI)-sponsored Netherlands Consortium for Healthy Aging (NCHA), Leiden, The Netherlands.
21. Interfaculty Institute for Genetics and Functional Genomics, Ernst-Moritz-Arndt University Greifswald, Greifswald, Germany.
22. Department of Pathology and Molecular Medicine, McMaster University, Hamilton, Ontario, Canada.

23. Division of Biomedical Statistics and Informatics, Mayo Clinic, Rochester, Minnesota, USA.
24. Department of Medicine II, University Medical Center Mainz, Mainz, Germany.
25. Department of Biostatistical Sciences, Wake Forest University, Division of Public Health Sciences, Winston-Salem, North Carolina, USA.
26. Department of Nutrition, Harvard School of Public Health, Boston, Massachusetts, USA.
27. Swiss Tropical and Public Health Institute, Basel, Switzerland.
28. University of Basel, Basel, Switzerland.
29. Division of Genetic Epidemiology, Innsbruck Medical University, Innsbruck, Austria.
30. Department of Medicine, University of Leipzig, Leipzig, Germany.
31. Medical Research Council Human Genetics Unit, Institute of Genetics and Molecular Medicine, Western General Hospital, Edinburgh, Scotland, UK.
32. Laboratory of Epidemiology, Demography and Biometry, National Institute on Aging, Bethesda, Maryland, USA.
33. Miami Institute for Human Genomics, Miami, Florida, USA.
34. McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA.
35. Human Genetics Center, University of Texas Health Science Center, Houston, Texas, USA.
36. Department of Epidemiology and Biostatistics, Department of Forensic Molecular Biology, Rotterdam, The Netherlands.
37. Department of Neurogeriatrics, Austrian Stroke Prevention Study, University Clinic of Neurology, Medical University Graz, Graz, Austria.
38. Laboratory of Neurogenetics, National Institute on Aging, Bethesda, Maryland, USA.
39. Clinical Research Branch, National Institute on Aging, Baltimore, Maryland, USA.
40. Kidney Research Institute and Division of Nephrology, University of Washington, Seattle, Washington, USA.
41. Medical Genetics Institute, Cedars-Sinai Medical Center, Los Angeles, California, USA.
42. Department of Biostatistics, University of Washington, Seattle, Washington, USA.
43. Department of Epidemiology, University of Washington, Seattle, Washington, USA.
44. Department of Medicine, Cardiovascular Health Research Unit, University of Washington and Group Health Research Institute, Seattle, Washington, USA.
45. Department of Epidemiology, University of Washington and Group Health Research Institute, Seattle, Washington, USA.
46. Department of Health Services, University of Washington, Seattle, Washington, USA.

47. Department of Internal Medicine, Erasmus University, Rotterdam, The Netherlands.
48. Department of Internal Medicine,Division of Nephrology and Hypertension, Mayo Clinic, Rochester, Minnesota, USA.
49. Institute for Medical Biometry and Statistics, University at Lübeck, Lübeck University Hospital Schleswig-Holstein, Campus Lübeck, Germany.
50. Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, Pennsylvania, USA.
51. Institute of Epidemiology, Helmholtz Zentrum München, German Research Center for Environmental Health, Neuherberg, Germany.
52. Institute of Medical Informatics, Biometry and Epidemiology, Ludwig-Maximilians-Universität, Munich, Germany.
53. Klinikum Grosshadern, Munich, Germany.
54. Zentrum für Innere Medizin, Klinik für Innere Medizin II–Kardiologie, Universitätsklinikum Ulm, Ulm, Germany.
55. Centre for Population Health Sciences, University of Edinburgh Medical School, Edinburgh, Scotland, UK.
56. Croatian Centre for Global Health, University of Split Medical School, Split, Croatia.
57. Andrija Stampar School of Public Health, Medical School, University of Zagreb, Zagreb, Croatia.
58. Department of Genetics and Pathology, Rudbeck Laboratory, Uppsala University, Uppsala, Sweden.
59. Institute of Clinical Molecular Biology, Christian-Albrechts-University, Kiel, Germany.
60. Department of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London, UK.
61. First Department of Internal Medicine, Paracelsus Medical University, Salzburg, Austria.
62. Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford, UK.
63. Oxford Centre for Diabetes, Endocrinology and Metabolism, University of Oxford, Oxford, UK.
64. Institute of Anatomy and Cell Biology, Ernst-Moritz-Arndt University Greifswald, Greifswald, Germany.
65. Institute for Community Medicine, Ernst-Moritz-Arndt University Greifswald, Greifswald, Germany.
66. Institute of Pharmacology, Ernst-Moritz-Arndt University Greifswald, Greifswald, Germany.
67. Institute of Clinical Chemistry and Laboratory Medicine, Ernst-Moritz-Arndt University Greifswald, Greifswald, Germany.
68. Amgen, Cambridge, Massachusetts, USA.
69. Brigham and Women's Hospital, Boston, Massachusetts, USA.
70. Department of Epidemiology, University of Michigan School of Public Health, Ann Arbor, Michigan, USA.
71. Department of Epidemiology and Prevention, Wake Forest University, Division of Public Health Sciences,

Winston-Salem, North Carolina, USA.
72. Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA.
73. University Hospitals of Geneva, Geneva, Switzerland.
74. School of Public Health and Family Medicine, Capital Medical University, Beijing, China.
75. Welch Center for Prevention, Epidemiology and Clinical Research, Johns Hopkins University, Baltimore, Maryland, USA.
76. General Internal Medicine, University of California, San Francisco, San Francisco, California, USA.
77. Department of Medicine V, Mannheim University Hospital, University of Heidelberg, Mannheim, Germany.
78. Institute of Physiology, Ernst-Moritz-Arndt University Greifswald, Greifswald, Germany.
79. Brigham and Women's Hospital Department of Endocrinology and Harvard Medical School, Boston, Massachusetts, USA.

II-c : Contributing authors in the Global Urate Genetics (GUGC) consortium.

The following studies participated in the discovery stage of the Global Urate Genetics (GUGC) consortium; AGES Reykjavik Study, Amish, ARIC, ASPS, AUSTWIN, BLSA, BRIGHT, CARDIA, CHS, CoLaus, CROATIA-KORCULA, CROATIA-SPLIT, CROATIA-VIS, DESIR, EPIC-Norfolk cohort, ERF, Estonian Biobank, Family Heart Study, Framingham Heart Study, Health 2000, InCHIANTI, INCIPE, INGI-Carlantino, INGI-CILENTO, INGI-FVG, INGI-Val Borbera, KORA F3, KORA F4, LBC1936, LifeLines, LOLIPOP, LURIC, MICROS, NESDA, NSPHS, ORCADES, PREVEND, PROCARDIS, RS-I, RS-II, SardiNIA, SHIP, SOCCS, Sorbs, TwinsUK, and Young Finns Study.

The following authors are participated in the GUGC consortium;

Anna Köttgen[1,2], Eva Albrecht[3], Alexander Teumer[4], Veronique Vitart[5], Jan Krumsiek[6], Claudia Hundertmark[1], Giorgio Pistis[7], Daniela Ruggiero[8], Conall M O'Seaghdha[9,10], Toomas Haller[11], Qiong Yang[9,12], Toshiko Tanaka[13], Andrew D Johnson[9], Zoltán Kutalik[14,15], Albert V Smith[16,17], Julia Shi[18], Maksim Struchalin[19], Rita PS Middelberg[20,21], Morris J Brown[22], Angelo L Gaffo[23,24], Nicola Pirastu[25], Guo Li[26], Caroline Hayward[5], Tatijana Zemunik[27], Jennifer Huffman[5], Loic Yengo[28,29], Jing Hua Zhao[30], Ayse Demirkan[31], Mary F Feitosa[32], Xuan Liu[12], Giovanni Malerba[33], Lorna M Lopez[34,35], Pim van der Harst[36], Xinzhong Li[37], Marcus E Kleber[38,39], Andrew A Hicks[40], Ilja M Nolte[41], Asa Johansson[42,43], Federico Murgia[44], Sarah H Wild[45], Stephan JL Bakker[46], John F Peden[47], Abbas Dehghan[19,48], Maristella Steri[49], Albert Tenesa[5,50], Vasiliki Lagou[51], Perttu Salo[52], Massimo Mangino[53], Lynda M Rose[54], Terho Lehtimäki[55], Owen M Woodward[56], Yukinori Okada[57,58], Adrienne Tin[2], Christian Müller[59], Christopher Oldmeadow[60], Margus Putku[61], Darina Czamara[62], Peter Kraft[63], Laura Frogheri[44], Gian Andri Thun[64,65], Anne Grotevendt[66], Gauti Kjartan Gislason[16], Tamara B Harris[67], Lenore J Launer[67], Patrick McArdle[18], Alan R Shuldiner[18], Eric Boerwinkle[68], Josef Coresh[2,69], Helena Schmidt[70],

Michael Schallert[71], Nicholas G Martin[21], Grant W Montgomery[21], Michiaki Kubo[72], Yusuke Nakamura[73], Toshihiro Tanaka[74], Patricia B Munroe[75], Nilesh J Samani[76,77], David R Jacobs Jr[78], Kiang Liu[79], Pio D'Adamo[25], Sheila Ulivi[80], Jerome I Rotter[81], Bruce M Psaty[26,82,83], Peter Vollenweider[84], Gerard Waeber[84], Susan Campbell[5], Olivier Devuyst[85], Pau Navaro[5], Ivana Kolcic[27], Nicholas Hastie[5], Beverley Balkau[86], Philippe Froguel[28,87], Tõnu Esko[11,61], Andres Salumets[11,88,89], Kay Tee Khaw[90], Claudia Langenberg[30], Nicholas J Wareham[30], Aaron Isaacs[31], Aldi Kraja[32], Qunyuan Zhang[32], Philipp S Wild[91,92], Rodney J Scott[93], Elizabeth G Holliday[60], Elin Org[61], Margus Viigimaa[94,95], Stefania Bandinelli[96], Jeffrey E Metter[13], Antonio Lupo[97], Elisabetta Trabetti[33], Rossella Sorice[8], Angela Döring[98,99], Eva Lattka[100], Konstantin Strauch[3,101], Fabian Theis[6], Melanie Waldenberger[100], H-Erich Wichmann[99,102,103], Gail Davies[34], Alan J Gow[34,35], Marcel Bruinenberg[104], LifeLines Cohort Study, Ronald P Stolk[105], Jaspal S Kooner[106,107], Weihua Zhang[107,108], Bernhard R Winkelmann[109], Bernhard O Boehm[110], Susanne Lucae[62], Brenda W Penninx[111-113], Johannes H Smit[111], Gary Curhan[114], Poorva Mudgal[63], Robert M Plenge[115,116], Laura Portas[44], Ivana Persico[44], Mirna Kirin[45], James F Wilson[45], Irene Mateo Leach[117], Wiek H van Gilst[117], Anuj Goel[47], Halit Ongen[47], Albert Hofman[19,48], Fernando Rivadeneira[118,119], Andre G Uitterlinden[118,119], Medea Imboden[64,65], Arnold von Eckardstein[120], Francesco Cucca[49], Ramaiah Nagaraja[121], Maria Grazia Piras[49], Matthias Nauck[66], Claudia Schurmann[4], Kathrin Budde[66], Florian Ernst[4], Susan M Farrington[5], Evropi Theodoratou[45], Inga Prokopenko[51], Michael Stumvoll[122,123], Antti Jula[124], Markus Perola[11,52,125], Veikko Salomaa[52], So-Youn Shin[126], Tim D Spector[53], Cinzia Sala[7], Paul M Ridker[54,127], Mika Kähönen[128], Jorma Viikari[129], Christian Hengstenberg[130], Christopher P Nelson[77,131], the CARDIoGRAM Consortium[132], the DIAGRAM Consortium, the ICBP Consortium, the MAGIC Consortium, James F Meschia[133], Michael A Nalls[134], Pankaj Sharma[135], Andrew B Singleton[134], Naoyuki Kamatani[136], Tanja Zeller[59], Michel Burnier[137], John Attia[60], Maris Laan[61], Norman Klopp[100], Hans L Hillege[36], Stefan Kloiber[62], Hyon Choi[114,138], Mario Pirastu[44], Silvia Tore[44], Nicole M Probst-Hensch[64,65], Henry Völzke[139], Vilmundur Gudnason[16,17], Afshin Parsa[18], Reinhold Schmidt[71], John B Whitfield[21], Myriam Fornage[140,141], Paolo Gasparini[25], David S Siscovick[26,142], Ozren Polasek[27], Harry Campbell[45], Igor Rudan[27,45], Nabila Bouatia-Naji[28], Andres Metspalu[11,61], Ruth JF Loos[30], Cornelia M van Duijn[31], Ingrid B Borecki[32,143], Luigi Ferrucci[13], Giovanni Gambaro[144], Ian J Deary[34,35], Bruce HR Wolffenbuttel[145], John C Chambers[107,108], Winfried März[39,146], Peter P Pramstaller[40], Harold Snieder[147], Ulf Gyllensten[43], Alan F Wright[5], Gerjan Navis[148], Hugh Watkins[47] on behalf of PROCARDIS, Jacqueline CM Witteman[19,48], Serena Sanna[49], Sabine Schipf[139], Malcolm G Dunlop[5], Anke Tönjes[122,123], Samuli Ripatti[125], Nicole Soranzo[126], Daniela Toniolo[7,149], Daniel I Chasman[54,127], Olli Raitakari[150], WH Linda Kao[2,69], Marina Ciullo[8], Caroline S Fox[9,151], Mark Caulfield[75], Murielle Bochud[152], Christian Gieger[3]

1. Renal Division, Freiburg University Hospital, Freiburg, Germany.
2. Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA.
3. Institute of Genetic Epidemiology, Helmholtz Zentrum München - German Research Center for Environmental Health, Neuherberg, Germany.
4. Interfaculty Institute for Genetics and Functional Genomics, Ernst-Moritz-Arndt-University Greifswald, Greifswald, Germany.
5. MRC Human Genetics Unit, MRC IGMM, University of Edinburgh, Edinburgh, UK.

6. Institute of Bioinformatics and Systems Biology, Helmholtz Zentrum München - German Research Center for Environmental Health, Neuherberg, Germany.
7. Division of Genetics and Cell Biology, San Raffaele Scientific Institute, Italy.
8. Institute of Genetics and Biophysics "A. Buzzati-Traverso" - CNR, Italy.
9. National Heart, Lung, and Blood Institute's Framingham Heart Study and Center for Population Studies, MA, USA.
10. Renal Division, Massachusetts General Hospital, Boston, MA, USA.
11. Estonian Genome Center, University of Tartu, Tartu, Estonia.
12. Department of Biostatistics, Boston University, MA, USA.
13. Clinical Research Branch, National Institute on Aging, Baltimore, MD, USA.
14. Department of Medical Genetics, University of Lausanne, Switzerland.
15. Swiss Institute of Bioinformatics, Lausanne, Switzerland.
16. Icelandic Heart Association Research Institute, Kopavogur, Iceland.
17. University of Iceland, Reykjavik, Iceland.
18. University of Maryland School of Medicine, Baltimore, MD, USA.
19. Department of Epidemiology, Erasmus Medical Center, Rotterdam, The Netherlands.
20. Department of Medicine, Prince Charles Hospital, Rode Road, Chermside, Queensland 4032, Australia.
21. Genetic Epidemiology, Queensland Institute of Medical Research, Brisbane, Australia.
22. University of Cambridge, UK.
23. Division of Rheumatology, University of Alabama at Birmingham, Birmingham, Alabama, USA.
24. Birmingham Veterans Affairs Medical Center, University of Alabama at Birmingham, Birmingham, Alabama, USA.
25. Institute for Maternal and Child Health - IRCCS "Burlo Garofolo"-Trieste, University of Trieste, Italy.
26. Cardiovascular Health Research Unit, University of Washington, Seattle, WA, USA.
27. Faculty of Medicine, University of Split, Croatia, Soltanska 2, Split, 21000, Croatia.
28. CNRS-UMR-8199, Genomics and Molecular Physiology of Metabolic Diseases, Institut Pasteur de Lille, France.
29. University Lille 1, Laboratory of Mathematics, CNRS-UMR 8524, MODAL team, INRIA Lille Nord-Europe, France.
30. MRC Epidemiology Unit, Institute of Metabolic Science, Addenbrooke's Hospital, Cambridge, UK.
31. Department of Epidemiology, Subdivision Genetic Epidemiology, Erasmus MC, Rotterdam, The Netherlands.
32. Division of Statistical Genomics, Department of Genetics, Washington University School of Medicine, St. Louis, MO, USA.
33. Biology and Genetics section, Department of Life and Reproduction Sciences, University of Verona, Italy.
34. Department of Psychology, The University of Edinburgh, Edinburgh, UK.

35. Centre for Cognitive Ageing and Cognitive Epidemiology, The University of Edinburgh, Edinburgh, UK.
36. Department of Cardiology, University Medical Center Groningen and University of Groningen, Groningen, The Netherlands.
37. Institute of Clinical Science, Faculty of Medicine, Imperial College London, UK.
38. LURIC Study nonprofit LLC, Freiburg, Germany.
39. Mannheim Institute of Public Health, Social and Preventive Medicine, Medical Faculty Mannheim, University of Heidelberg, Mannheim, Germany.
40. Center for Biomedicine, European Academy Bozen/Bolzano (EURAC), Bolzano, Italy. Affiliated Institute of the University of Lübeck, Germany.
41. Unit of Genetic Epidemiology and Bioinformatics, Department of Epidemiology, University Medical Center Groningen, University of Groningen, The Netherlands.
42. Uppsala Clinical Research Center, Uppsala University Hospital, Sweden.
43. Department of Immunology, Genetics and Pathology, Rudbeck Laboratory, Uppsala University, Uppsala, 751 85, Sweden.
44. Institute of Population Genetics - CNR, Italy.
45. Centre for Population Health Sciences, The University of Edinburgh Medical School, Edinburgh, Scotland, UK.
46. Department of Internal Medicine, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands.
47. Department of Cardiovascular Medicine, Wellcome Trust Centre for Human Genetics, University of Oxford, UK.
48. Member of Netherlands Consortium for Healthy Aging (NCHA) sponsored by Netherlands Genomics Initiative (NGI), Leiden, The Netherlands.
49. Istituto di Ricerca Genetica e Biomedica, Consiglio Nazionale delle Ricerche, Monserrato, Cagliari, Italy.
50. Roslin Institute. The University of Edinburgh, UK.
51. Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford, UK.
52. Department of Chronic Disease Prevention, National Institute for Health and Welfare (THL), Helsinki, Finland.
53. King's College London, St. Thomas' Hospital Campus, London, UK.
54. Preventive Medicine, Brigham and Women's Hospital, Boston, MA, USA.
55. University of Tampere and Tampere University Hospital, Tampere, Finland.
56. Department of Physiology, Johns Hopkins University, School of Medicine, Baltimore, MD, USA.
57. Laboratory for Statistical Analysis, Center for Genomic Medicine, RIKEN, Japan.
58. Department of Allergy and Rheumatology, Graduate School of Medicine, University of Tokyo, Tokyo, Japan.
59. University Heart Center Hamburg, Clinic for general and interventional Cardiology, Hamburg, Germany.

60. School of Medicine and Public Health, University of Newcastle, Australia.
61. Institute of Molecular and Cell Biology, University of Tartu, Tartu, Estonia.
62. Max Planck Institute of Psychiatry, Munich, Germany.
63. Program in Molecular and Genetic Epidemiology, Harvard School of Public Health, Boston, MA, USA.
64. Swiss Tropical and Public Health Institute, Basel, Switzerland.
65. University of Basel, Basel, Switzerland.
66. Institute of Clinical Chemistry and Laboratory Medicine, University Medicine Greifswald, Ernst-Moritz-Arndt University Greifswald, Greifswald, Germany.
67. Laboratory of Epidemiology, Demography and Biometry, National Institute on Aging, Bethesda, MD, USA.
68. University of Texas Health Science Center at Houston, TX, USA.
69. Welch Center for Prevention, Epidemiology and Clinical Research, John Hopkins University, Baltimore, MD, USA.
70. Institute of Molecular Biology and Biochemistry, Medical University Graz, Austria.
71. Department of Neurology, Section of Special Neurology, Medical University Graz, Austria.
72. Laboratory for Genotyping Development, Center for Genomic Medicine, RIKEN, Japan.
73. Laboratory of Molecular Medicine, Human Genome Center, Institute of Medical Science, University of Tokyo, Japan.
74. Laboratory for Cardiovascular Diseases, Center for Genomic Medicine, RIKEN, Japan.
75. William Harvey Research Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, UK.
76. Leicester NIHR Biomedical Research Unit in Cardiovascular Disease, Glenfield Hospital, Leicester, UK.
77. Department of Cardiovascular Sciences, University of Leicester, Leicester, UK.
78. Division of Epidemiology and Community Health, University of Minnesota, Minneapolis, MN, USA.
79. Department of Preventive Medicine, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA.
80. Intitute for Maternal and Child Health - IRCCS "Burlo Garofolo" - Trieste, Italy.
81. Medical Genetics Institute, Cedars-Sinai Medical Center, Los Angeles, CA, USA.
82. Group Health Research Institute, Group Health Cooperative, Seattle, WA, USA.
83. Departments of Medicine, Epidemiology and Health Services, University of Washington, Seattle, WA, USA.
84. Department of Medicine, Internal Medicine, Lausanne University Hospital, Lausanne, Switzerland.
85. Institute of Physiology, Zurich Center for Integrative Human Physiology (ZIHP), University of Zurich, Switzerland.
86. University Paris Sud 11, UMRS 1018, Villejuif, France.
87. Department of Genomics of Common Disease, School of Public Health, Imperial College London, Hammersmith Hospital, London, UK.

88. Competence Centre on Reproductive Medicine and Biology, Tartu, Estonia.
89. Department of Obstetrics and Gynecology, University of Tartu, Tartu, Estonia.
90. Clinical Gerontology Unit, Addenbrooke's Hospital, Cambridge, UK.
91. Department of Medicine II , University Medical Center Mainz, Johannes Gutenberg University Mainz, Germany.
92. Center for Thrombosis and Hemostasis, University Medical Center Mainz, Johannes Gutenberg University Mainz, Germany.
93. School of Biomedical Sciences and Pharmacy, University of Newcastle, Australia.
94. Tallinn University of Technology, Department of Biomedical Engineering, Chair of Medical Physics, Tallinn, Estonia.
95. Centre of Cardiology, North Estonia Medical Centre, Tallinn, Estonia
96. Geriatric Unit, Azienda Sanitaria Firenze (ASF), Florence, Italy.
97. Division of Nephrology, Department of Medicine, University of Verona, Italy.
98. Institute of Epidemiology II, Helmholtz Zentrum München - German Research Center for Environmental Health, Neuherberg, Germany.
99. Institute of Epidemiology I, Helmholtz Zentrum München - German Research Center for Environmental Health, Neuherberg, Germany.
100. Research Unit of Molecular Epidemiology, Helmholtz Zentrum München - German Research Center for Environmental Health, Neuherberg, Germany.
101. Institute of Medical Informatics, Biometry and Epidemiology, Chair of Genetic Epidemiology, Ludwig-Maximilians-University, Munich, Germany.
102. Institute of Medical Informatics, Biometry and Epidemiology, Chair of Epidemiology, Ludwig-Maximilians-University, Munich, Germany.
103. Klinikum Grosshadern, Munich, Germany.
104. University Medical Center Groningen and University of Groningen, The Netherlands.
105. Department of Epidemiology, University Medical Center Groningen and University of Groningen, The Netherlands.
106. Faculty of Medicine, National Heart & Lung Institute, Cardiovascular Science, Hammersmith Hospital, Hammersmith Campus, Imperial College London, UK.
107. Cath Lab, Cardiology, Ealing Hospital, Southall, Middlesex, UK.
108. Department of Epidemiology and Biostatistics, School of Public Health, Imperical College London, UK.
109. Cardiology Group, Frankfurt-Sachsenhausen, Germany.
110. Division of Endocrinology and Diabetes, Department of Medicine, University Hospital, Ulm, Germany.
111. Department of Psychiatry/EMGO Institute, VU University Medical Centre, Amsterdam, the Netherlands.
112. Department of Psychiatry, University Medical Centre Groningen, University of Groningen, Groningen, the Netherlands.
113. Department of Psychiatry, Leiden University Medical Center, Leiden, the Netherlands.

114. Channing Laboratory, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA.
115. Brigham and Women's Hospital, Division of Rheumatology, Immunology and Allergy, Division of Genetics, Boston, MA, USA.
116. Broad Institute of MIT and Harvard, Cambridge, MA, USA.
117. Division of Experimental Cardiology, Department of Cardiology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands.
118. Department of Internal Medicine, Erasmus Medical Center, Rotterdam, The Netherlands.
119. Department of Epidemiology, Erasmus Medical Center, Rotterdam, The Netherlands + Member of Netherlands Consortium for Healthy Aging (NCHA) sponsored by Netherlands Genomics Initiative (NGI), Leiden, The Netherlands.
120. Institute of Clinical Chemistry, University Hospital of Zurich, Zurich, Switzerland.
121. Laboratory of Genetics, National Institute on Aging, Baltimore, MD, USA.
122. Medical Department, University of Leipzig, Leipzig, Germany.
123. IFB AdiposityDiseases, University of Leipzig, Leipzig, Germany.
124. Department of Chronic Disease Prevention, National Institute for Health and Welfare (THL), Turku, Finland.
125. University of Helsinki, Institute of Molecular Medicine, Helsinki, Finland.
126. Human Genetics, Wellcome Trust Sanger Institute, Hinxton, UK.
127. Harvard Medical School, Boston, MA, USA.
128. Department of Clinical Physiology, University of Tampere and Tampere University Hospital, Tampere, Finland.
129. Department of Medicine, University of Turku, and Turku University Hospital, Turku, Finland.
130. University Hospital Regensburg, Regensburg, Germany.
131. NIHR Cardiovascular Biomedical Research Unit, Glenfield Hospital, Leicester, UK.
132. A full list of CARDIoGRAM Consortium members can be found in the Supplementary Materials.
133. Department of Neurology, Mayo Clinic, Jacksonville, FL, USA.
134. Molecular Genetics Section, Laboratory of Neurogenetics, NIA, NIH, Bethesda, MD, USA.
135. Imperial College Cerebrovascular Research Unit, Imperial College London, London, UK.
136. Laboratory for International Alliance, Center for Genomic Medicine, RIKEN, Japan.
137. Department of Medicine, Nephrology Division, Lausanne University Hospital, Lausanne, Switzerland.
138. Section of Rheumatology and the Clinical Epidemiology Unit, Boston University School of Medicine, Boston, MA, USA.
139. Institute for Community Medicine, University Medicine Greifswald, Greifswald, Germany.
140. University of Texas - Houston Institute of Molecular Medicine, TX, USA.
141. University of Texas - Houston School of Public Health, TX, USA.
142. Departments of Medicine and Epidemiology, University of Washington, Seattle, WA, USA.
143. Division of Biostatistics, Washington University School of Medicine, Saint Louis, MO, USA.

144. Institute of Internal Medicine, Renal Program, Columbus-Gemelli University Hospital, Catholic University, Rome, Italy.
145. Department of Endocrinology, University Medical Center Groningen and University of Groningen, The Netherlands.
146. Synlab Centre of Laboratory Diagnostics, Heidelberg, Germany.
147. Department of Epidemiology, University Medical Center Groningen, University of Groningen, The Netherlands.
148. Division of Nephrology, Department of Internal Medicine, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands.
149. Institute of Molecular Genetics-CNR, Pavia, Italy.
150. Research Centre of Applied and Preventive Cardiovascular Medicine, University of Turku and the Department of Clinical Physiology and Nuclear Medicine, Turku University Hospital, Turku, Finland.
151. Division of Endocrinology, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA.
152. University Institute of Social and Preventive Medicine, Lausanne, Switzerland.

REFERENCES

1. Nakamura Y. The BioBank Japan Project. *Clin Adv Hematol Oncol* **5**, 696-697 (2007).
2. Kamatani Y et al. Genome-wide association study of hematological and biochemical traits in a Japanese population. *Nat Genet* **42**, 210-215 (2010).
3. Okada Y et al. Genome-wide association study for C-reactive protein levels identified pleiotropic associations in the IL6 locus. *Hum Mol Genet* **20**, 1224-1231 (2011).
4. Okada Y et al. Identification of nine novel loci associated with white blood cell subtypes in a Japanese population. *PLoS Genet* **7**, e1002067 (2011).
5. Okada Y et al. Common variants at CDKAL1 and KLF9 are associated with body mass index in east Asian populations. *Nat Genet* **44**, 302-306 (2012).
6. Kato N et al. Meta-analysis of genome-wide association studies identifies common variants associated with blood pressure variation in east Asians. *Nat Genet* **43**, 531-538 (2011).
7. Hughes K et al. Cardiovascular diseases in Chinese, Malays, and Indians in Singapore. II. Differences in risk factor levels. *J Epidemiol Community Health* **44**, 29-35 (1990).
8. Tan CE, Emmanuel SC, Tan BY, Jacob E. Prevalence of diabetes and ethnic differences in cardiovascular risk factors. The 1992 Singapore National Health Survey. *Diabetes Care* **22**, 241-247 (1999).
9. Hughes K, Aw TC, Kuperan P, Choo M. Central obesity, insulin resistance, syndrome X, lipoprotein(a), and cardiovascular risk in Indians, Malays, and Chinese in Singapore. *J Epidemiol Community Health* **51**, 394-399 (1997).
10. Cutter J, Tan BY, Chew SK. Levels of cardiovascular disease risk factors in Singapore following a national intervention programme. *Bull World Health Organ* **79**, 908-915 (2001).
11. Foong AW et al. Rationale and methodology for a population-based study of eye diseases in Malay people: The Singapore Malay eye study (SiMES). *Ophthalmic Epidemiol* **14**, 25-35 (2007).
12. Lavanya R et al. Methodology of the Singapore Indian Chinese Cohort (SICC) eye study: quantifying ethnic variations in the epidemiology of eye diseases in Asians. *Ophthalmic Epidemiol* **16**, 325-336 (2009).
13. Cho YS et al. A large-scale genome-wide association study of Asian populations uncovers genetic factors influencing eight quantitative traits. *Nat Genet* **41**, 527-534 (2009).
14. Kim YJ et al. Large-scale genome-wide association studies in east Asians identify new genetic loci influencing metabolic traits. *Nat Genet* **43**, 990-995 (2011).
15. Pan WH et al. Han Chinese cell and genome bank in Taiwan: purpose, design and ethical considerations. *Hum Hered* **61**, 27-30 (2006).

16. Tsai FJ et al. A genome-wide association study identifies susceptibility variants for type 2 diabetes in Han Chinese. *PLoS Genet* **6**, e1000847 (2010).
17. Lin HJ et al. Single-nucleotide polymorphisms in chromosome 3p14.1- 3p14.2 are associated with susceptibility of type 2 diabetes with cataract. *Mol Vis* **16**, 1206-1214 (2010).
18. GenSalt Collaborative Research Group. GenSalt: rationale, design, methods and baseline characteristics of study participants. *J Hum Hypertens* **21**, 639-646 (2007).
19. Takeuchi F et al. Blood pressure and hypertension are associated with 7 loci in the Japanese population. *Circulation* **121**, 2302-2309 (2010).
20. Takeuchi F et al. Confirmation of multiple risk Loci and genetic impacts by a genome-wide association study of type 2 diabetes in the Japanese population. *Diabetes* **58**, 1690-1699 (2009).
21. Yamaguchi-Kabata Y et al. Japanese population structure, based on SNP genotypes from 7003 individuals compared to other ethnic groups: effects on population-based association studies. *Am J Hum Genet* **83**, 445-456 (2008).
22. Horio M, Imai E, Yasuda Y, Watanabe T, Matsuo S. Modification of the CKD epidemiology collaboration (CKD-EPI) equation for Japanese: accuracy and use for population estimates. *Am J Kidney Dis* **56**, 32-38 (2010).
23. Devlin B, Roeder K. Genomic control for association studies. *Biometrics* **55**, 997-1004 (1999).
24. de Bakker PI et al. Practical aspects of imputation-driven meta-analysis of genome-wide association studies. *Hum Mol Genet* **17**, R122-R128 (2008).
25. Chambers JC et al. Genetic loci influencing kidney function and chronic kidney disease. *Nat Genet* **42**, 373-375 (2010).
26. Gudbjartsson DF et al. Association of variants at UMOD with chronic kidney disease and kidney stones-role of age and comorbid diseases. *PLoS Genet* **6**, e1001039 (2010).
27. Köttgen A et al. New loci associated with kidney function and chronic kidney disease. *Nat Genet* **42**, 376-384 (2010).
28. Köttgen A et al. Multiple loci associated with indices of renal function and chronic kidney disease. *Nat Genet* **41**, 712-717 (2009).
29. Albrecht E et al. Common variants identified by meta-analysis of 110,238 individuals associate with serum urate. *60th Annual Meeting of the American Society of Human Genetics* (2011).
30. Li S et al. The GLUT9 gene is associated with serum uric acid levels in Sardinia and Chianti cohorts. *PLoS Genet* **3**, e194 (2007).
31. Wallace C et al. Genome-wide association study identifies genes for biomarkers of cardiovascular disease: serum urate and dyslipidemia. *Am J Hum Genet* **82**, 139-149 (2008).

32. Döring A et al. SLC2A9 influences uric acid concentrations with pronounced sex-specific effects. *Nat Genet* **40**, 430-436 (2008).
33. Dehghan A et al. Association of three genetic loci with uric acid concentration and risk of gout: a genome-wide association study. *Lancet* **372**, 1953-1961 (2008).
34. Vitart V et al. SLC2A9 is a newly identified urate transporter influencing serum urate concentration, urate excretion and gout. *Nat Genet* **40**, 437-442 (2008).
35. Kolz M et al. Meta-analysis of 28,141 individuals identifies common variants within five new loci that influence uric acid concentrations. *PLoS Genet* **5**, e1000504 (2009).
36. Yang Q et al. Multiple genetic loci influence serum urate levels and their relationship with gout and cardiovascular disease risk factors. *Circ Cardiovasc Genet* **3**, 523-530 (2010).
37. Johnson AD et al. SNAP: a web-based tool for identification and annotation of proxy SNPs using HapMap. *Bioinformatics* **24**, 2938-2939 (2008).
38. Price AL et al. Principal components analysis corrects for stratification in genome-wide association studies. *Nat Genet* **38**, 904-909 (2006).
39. The International HapMap Consortium. The International HapMap Project. *Nature* **426**, 789-796 (2003).
40. Li Y, Willer CJ, Ding J, Scheet P, Abecasis GR. MaCH: using sequence and genotype data to estimate haplotypes and unobserved genotypes. *Genet Epidemiol* **34**, 816-834 (2010).
41. Nang EE et al. Is there a clear threshold for fasting plasma glucose that differentiates between those with and without neuropathy and chronic kidney disease?: the Singapore Prospective Study Program. *Am J Epidemiol* **169**, 1454-1462 (2009).
42. Sim X et al. Transferability of type 2 diabetes implicated loci in multi-ethnic cohorts from Southeast Asia. *PLoS Genet* **7**, e1001363 (2011).
43. Teo YY et al. Singapore Genome Variation Project: a haplotype map of three Southeast Asian populations. *Genome Res* **19**, 2154-2162 (2009).
44. Marchini J, Howie B, Myers S, McVean G, Donnelly P. A new multipoint method for genome-wide association studies by imputation of genotypes. *Nat Genet* **39**, 906-913 (2007).
45. Howie BN, Donnelly P, Marchini J. A flexible and accurate genotype imputation method for the next generation of genome-wide association studies. *PLoS Genet* **5**, e1000529 (2009).
46. Levey AS, Greene T, Kusek JW. A simplified equation to predict glomerular filtration rate from serum creatinine. *J Am Soc Nephrol* **11**, 155A (2000).
47. Purcell S et al. PLINK: a tool set for whole-genome association and population-based linkage analyses. *Am J Hum Genet* **81**, 559-575 (2007).
48. Abecasis GR, Cherny SS, Cookson WO, Cardon LR. GRR: graphical representation of relationship

errors. *Bioinformatics* **17**, 742-743 (2001).

49. O'Connell JR, Weeks DE. PedCheck: a program for identification of genotype incompatibilities in linkage analysis. *Am J Hum Genet* **63**, 259-266 (1998).

50. Browning BL, Browning SR. A unified approach to genotype imputation and haplotype-phase inference for large data sets of trios and unrelated individuals. *Am J Hum Genet* **84**, 210-223 (2009).