

Supplementary Table 1. Baseline demographics according to race/ethnicity.

	African American N=712	Chinese N=718	Caucasian N=712	Hispanic N=705	Combined N=2847
Age (years)	62±10	62±10	61±10	61±10	62±10
Female (%)	55	52	53	54	53
Hypertension (%)	56	37	39	42	44
Diabetes (%)	28	23	13	31	24
Mean MDRD eGFR, mL/min/1.73m ²	84±19	80±16	75±20	80±18	80±18
MDRD eGFR <60 (%)	7	10	14	8	10
Median UAE, mg/g	5.2 (3.2, 12.4)	6.8 (4.0, 12.8)	4.5 (3.1, 8.3)	6.2 (3.8, 12.8)	5.6 (3.4, 11.6)
UAE ≥17/25 mg/g (%)*	16	17	10	16	15
Mean cystatin C eGFR, mL/min/1.73m ²	93±24	91±21	85±19	85±20	88±22
Cystatin C eGFR <60 (%)	6	6	11	9	8

mean values ± standard distribution or percent distribution or median values with interquartile range
eGFR= estimated GFR; UAE= urine albumin excretion.

* UAE ≥ 17 mg/g in men or ≥ 25 mg/g in women.

Supplementary Table 2. Single nucleotide polymorphisms in the ACE, AGT, AGTR1, and AGTR2 genes.

This table displays the single nucleotide polymorphisms as well as the function, minor and major alleles, and minor allele frequencies of these polymorphisms. The minor allele was based on the combined analysis.

	SNP	Function	Major Allele	Minor Allele	Minor Allele Frequency				
					Combined	African American	Chinese	Caucasian	Hispanic
ACE									
1	rs4291	noncoding	T	A	0.35	0.35	0.36	0.36	0.32
2	rs4295	noncoding	G	C	0.37	0.42	0.35	0.36	0.34
3	rsMESA03†	coding, nonsynonymous	G	A	0.003	0.01	0	0	0.0007
4	rs4303 (A261S)	coding, nonsynonymous	C	A	0.02	0.07	0	0.0007	0.01
5	rs4305	noncoding	A	G	0.50	0.22	0.64	0.56	0.57
6	rs4309	coding, synonymous	G	A	0.44	0.19	0.66	0.42	0.48
7	rs4311	noncoding	G	A	0.37	0.25	0.34	0.48	0.40
8	rs12720746 (V524A)	coding, nonsynonymous	A	G	0.0004	0	0	0	0.001
9	rs12709426 (D592G)	coding, nonsynonymous	A	G	0.01	0.04	0	0	0.01
10	rs4316	noncoding	A	G	0.49	0.60	0.33	0.54	0.50
11	rs4351	noncoding	A	G	0.47	0.47	0.40	0.53	0.46
12	rs4353	noncoding	A	G	0.50	0.41	0.60	0.47	0.51
13	rs4976 (I444T)	coding, nonsynonymous	A	G	0.0005	0.001	0.0007	0	0
14	rs4359	noncoding	G	A	0.46	0.43	0.40	0.54	0.47
15	rs4362	coding, synonymous	G	A	0.45	0.43	0.40	0.53	0.45
16	rs4363	noncoding	A	G	0.46	0.43	0.40	0.54	0.46
17	rs4980 (R1279Q)	coding, nonsynonymous	G	A	0.003	0.00	0	0.005	0.004
18	rs4461142	noncoding	G	A	0.37	0.18	0.42	0.48	0.40
19	rs4459610 (K715N)	coding, nonsynonymous	A	G	0.46	0.57	0.27	0.57	0.45
20	rs8066276	noncoding	A	G	0.42	0.36	0.27	0.61	0.45
21	rs4277404	noncoding	G	A	0.02	0.01	0	0.06	0.03
22	rs4968591	noncoding	A	G	0.27	0.18	0.22	0.40	0.30
AGT									
1	rs7536290	noncoding	A	G	0.26	0.35	0.25	0.15	0.30
2	rs943580	noncoding	G	A	0.31	0.19	0.16	0.59	0.31
3	rs5044	noncoding	A	C	0.003	0.01	0	0	0.002
4	rs3789670	noncoding	G	A	0.16	0.23	0.20	0.10	0.12
5	rs3789671	noncoding	C	A	0.34	0.36	0.54	0.18	0.28
6	rs2478545	noncoding	G	A	0.34	0.45	0.30	0.23	0.38
7	rs699 (M235T)#	coding, nonsynonymous	C	T	0.32	0.20	0.16	0.59	0.34*
8	rs2148582	noncoding	G	A	0.32	0.20	0.16	0.57	0.33*
9	rs7549009	noncoding	G	A	0.30	0.31	0.49	0.10	0.30
10	rs1326886	noncoding	A	G	0.26	0.17	0.49	0.10	0.28*
AGTR1									
1	rs409742	noncoding	A	G	0.18	0.23	0.12	0.21	0.16
2	rs422858	noncoding	A	C	0.17	0.23	0.09	0.21	0.16
3	rs2638363	noncoding	G	A	0.20	0.34	0.09	0.21	0.17
4	rs2131127	noncoding	G	A	0.44	0.68	0.39	0.33	0.37
5	rs2638360	noncoding	A	G	0.10	0.03	0.07	0.20	0.09
6	rs4681443	noncoding	G	A	0.27	0.61	0.07	0.17	0.22*
7	rs718858	noncoding	G	A	0.16	0.24	0.07	0.17	0.14

8	rs3772616	noncoding	G A	0.36	0.70	0.19	0.18	0.38
9	rs4488792	noncoding	G A	0.32	0.61	0.14	0.17	0.35
10	rs389566	noncoding	A T	0.33	0.61	0.14	0.27	0.28
11	rs385338	noncoding	G C	0.26	0.51	0.14	0.18	0.21
12	rs6801836	noncoding	A G	0.24	0.37	0.11	0.24	0.23
13	rs2320019	noncoding	A G	0.12	0.36	0	0.05	0.09
14	rs275646	noncoding	G A	0.07	0.05	0.15	0.04	0.04
15	rs275645	noncoding	A G	0.50	0.70	0.23	0.45	0.50

AGTR2

1	rs5950584	noncoding	A C	0.12	0.40	0	0.004	0.09*
2	rs5950586	noncoding	G A	0.01	0.03	0	0	0.01
3	rs1403543	noncoding	A G	0.48	0.36	0.43	0.49	0.38
4	rs5190	coding, synonymous	A G	0.01	0.01	0	0	0.01
5	rs5191 (R248K)	coding, nonsynonymous	G A	0.01	0.03	0	0	0.01
6	rs6608590	noncoding	G A	0.47	0.40	0.41	0.48	0.37

* not in Hardy-Weinberg equilibrium.

For the M235T polymorphism, the Illumina panel reports an A/G polymorphism. However, the polymorphism has been previously reported as a C/T polymorphism. This discrepancy is due to the forward strand vs. reverse strand analysis.

8	rs2148582	0.24	0.07	0.27	0.12	0.06	0.01†	0.52	0.99	0.27	0.23	0.19	0.04†	0.99	0.51	0.55	0.55	0.15	0.37	HWE	HWE	HWE	HWE	HWE	HWE	0.29	0.16	0.35	0.21	0.008	0.001^
9	rs7549009	0.86	0.43	0.91	0.38	0.33	0.88	0.92	0.66	0.87	0.88	0.50	0.68	0.19	0.52	0.75	0.97	0.71	0.09	0.23	0.31	0.80	0.07	0.95	0.56	0.26	0.52	0.95	0.70	0.30	0.50
10	rs1326886	0.36	0.53	0.33	0.60	0.51	0.71	0.98	0.79	0.96	0.88	0.52	0.66	0.77#	0.70#	0.81#	0.78#	0.81#	0.24#	HWE	HWE	HWE	HWE	HWE	HWE	0.50	0.35	0.54	0.69	0.26	0.13
AGTR1																															
1	rs409742	0.57	0.19	0.86	0.43	0.55	0.85	0.86	0.36	0.69	0.48	0.91	0.89	0.39	0.66	0.33	0.70	0.25	0.76	0.79	0.77	0.78	0.25	0.19	0.87	0.92	0.14	0.61	0.26	0.79	0.92
2	rs422858	0.61	0.42	0.84	0.20	0.29	0.93	0.41#	0.74#	0.37#	0.88#	0.91#	0.77#	0.42	0.76	0.28	0.75	0.33	0.65	0.73	0.93	0.59	0.31	0.26	0.96	0.73	0.59	0.33	0.33	0.76	0.93
3	rs2638363	0.66	0.04†	0.78	0.04†	0.76	0.60	0.27#	1.00#	0.33#	0.84#	0.33#	0.27#	0.42	0.79	0.24	0.73	0.31	0.67	0.77	0.70	0.78	0.45	0.24	0.85	0.97	0.15	0.36	0.17	0.59	0.43
4	rs2131127	0.22	0.03†	0.06	0.02†	0.56	0.72	0.30	0.87	0.68	0.04†	0.96	0.66	0.91	0.18	0.48	0.20	0.17	0.22	0.30	0.06	0.31	0.002†	0.09	0.83	0.11	0.15	0.05	0.002	0.90	0.58
5	rs2638360	0.53#	0.50#	0.06#	0.22#	0.53#	0.95#	0.57#	0.91#	0.67#	0.65#	0.46#	0.36#	0.70	0.99	0.30	0.99	0.51	0.82	0.37#	0.67#	0.27#	0.59#	0.01#†	0.02#†	0.75	0.66	0.72	0.59	0.36	0.17
6	rs4681443	0.36	0.05	0.21	0.02	0.92	0.50	0.66#	0.13#	0.88#	0.70#	0.43#	0.97#	0.12	0.23	0.18	0.67	0.91	0.58	HWE	HWE	HWE	HWE	HWE	HWE	0.53	0.65	0.91	0.21	0.71	1.00
7	rs718858	0.15	0.10	0.70	0.15	0.42	0.53	0.66#	0.13#	0.88#	0.70#	0.43#	0.97#	0.19	0.19	0.26	0.62	0.61	0.41	0.23	0.31	0.20	0.0001†	0.09	0.40	0.66	0.91	0.69	0.01	0.60	0.71
8	rs3772616	0.37	0.12	0.14	0.18	0.03†	0.06	0.88	0.83	0.57	0.17	0.63	0.28	0.89	0.11	0.36	0.93	0.69	0.45	0.95	0.24	0.66	0.05	0.06	0.03†	0.67	0.65	0.82	0.33	0.12	0.27
9	rs4488792	0.52	0.11	0.54	0.45	0.21	0.31	0.19	0.33	0.19	0.67	0.87	0.57	0.98	0.13	0.34	0.86	0.78	0.47	0.77	0.28	0.78	0.03†	0.02†	0.02†	0.61	0.92	0.34	0.17	0.08	0.33
10	rs389566	0.60	0.34	0.17	0.41	0.92	0.95	0.27	0.86	0.73	0.79	0.11	0.64	0.58	0.82	0.24	0.24	0.78	0.18	0.92	0.67	0.89	0.97	0.63	1.00	0.56	0.78	0.17	0.27	0.34	0.69
11	rs385338	0.44	0.44	0.25	0.22	0.94	0.66	0.27	0.96	0.95	0.98	0.13	0.57	0.71	0.73	0.29	0.56	0.78	0.30	0.93	0.68	0.10	0.11	0.66	0.59	0.42	0.99	0.74	0.90	0.43	0.78
12	rs6801836	0.34	0.60	0.90	0.33	0.75	0.92	0.45	0.95	0.71	0.30	0.19	0.68	0.67	0.68	0.13	0.51	0.51	0.24	0.89	0.92	0.40	0.93	0.88	0.66	0.81	0.66	0.20	0.20	0.68	0.52
13	rs2320019	0.02†	0.02†	0.05	0.10	0.72	0.53	NP	NP	NP	NP	NP	NP	0.45#	0.09#	0.03#†	0.35#	0.86#	0.17#	0.53#	0.44#	0.60#	0.30#	0.86#	0.91#	0.03	0.003	0.77	0.77	0.96	0.82
14	rs275646	0.21#	0.35#	0.83#	0.79#	0.007†	0.02†	0.75	0.43	0.49	0.89	0.10	0.32	0.43#	0.26#	0.58#	0.58#	0.09#	0.21#	0.56#	0.44#	0.15#	0.07#	0.02#†	0.13#	0.22	0.38	0.43	0.37	0.89	0.61
15	rs275645	0.94	0.48	0.54	0.17	0.50	0.18	0.53	0.36	0.90	0.44	0.66	0.96	0.05	0.10	0.58	0.65	0.61	0.70	0.87	0.56	0.70	0.22	0.70	0.77	0.16	0.66	0.77	0.93	0.91	0.76
AGTR2																															
1M	rs5950584 – M	0.43	0.34	0.08	0.31	0.28	0.21	NP	NP	NP	NP	NP	NP	0.30	0.08	0.40	0.99	0.00008†	0.99	0.83	0.52	0.99	0.41	0.14	0.21	0.24	0.16	0.60	0.84	0.0002^	0.16
1F	rs5950584 – F	0.39	0.21	0.60	0.28	0.06	0.31	NP	NP	NP	NP	NP	NP	0.36#	0.99#	0.14#	0.99#	0.98#	0.99#	HWE	HWE	HWE	HWE	HWE	HWE	0.79	0.52	0.19	0.37	0.29	0.46
2M	rs5950586 – M	0.42	0.59	0.64	0.46	0.33	0.61	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	0.81	0.99	0.75	0.99	0.48	0.99	0.46	0.84	0.58	0.70	0.84	0.77
2F	rs5950586 – F	0.79#	0.06#	0.85#	0.34#	0.25#	0.56#	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	0.51#	0.68#	0.60#	0.62#	0.94#	0.52#	0.51	0.31	0.61	0.31	0.38	0.97
3M	rs1403543 – M	0.33	0.41	0.50	0.94	0.40	0.29	0.64	0.61	0.81	0.80	0.82	0.61	0.95	0.59	0.48	0.85	0.79	0.71	0.90	0.29	0.48	0.51	0.36	0.79	0.88	0.29	0.83	0.73	0.26	0.88
3F	rs1403543 – F	0.29	0.71	0.31	0.32	0.88	0.73	0.03†	0.02†	0.08	0.25	0.49	0.44	0.74	0.92	0.58	0.49	0.05	0.05	0.14	0.05†	0.46	0.26	0.81	0.95	0.98	0.78	0.77	0.89	0.56	0.47
4M	rs5190 – M	0.10	0.24	0.60	0.19	0.66	0.99	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	0.19	0.16	0.18	0.23	0.29	0.99	0.04	0.07	0.19	0.08	0.29	0.98
4F	rs5190 – F	0.001#†	0.31#	0.31#	0.42#	0.58#	0.67#	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	0.36#	0.40#	0.50#	0.95#	0.81#	0.98#	0.004	0.19	0.23	0.54	0.58	0.75
5M	rs5191 (R248K) – M	0.79	0.39	0.68	0.98	0.13	0.36	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	0.21	0.99	0.98	0.99	0.67	0.50	0.49	0.51	0.76	0.98	0.17	0.35
5F	rs5191 (R248K) – F	0.29#	0.33#	0.44#	0.73#	0.55#	0.71#	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	0.16#	0.18#	0.82#	0.61#	0.11#	1.00#	0.80	0.79	0.69	0.90	0.48	0.79
6M	rs6608590 – M	0.81	0.77	0.84	0.40	0.80	0.33	0.70	0.62	0.91	0.94	0.71	0.47	0.89	0.74	0.65	0.93	0.58	0.85	0.93	0.29	0.67	0.35	0.32	0.82	0.85	0.40	0.95	0.32	0.41	0.88
6F	rs6608590 – F	0.97	0.68	0.29	0.51	0.37	0.83	0.01†	0.01†	0.10	0.21	0.41	0.23	0.72	0.85	0.61	0.52	0.03†	0.06	0.02†	0.01†	0.28	0.12	0.75	0.58	0.80	0.94	0.99	0.61	0.93	0.61

MAF <10%

NP not polymorphic

† Association confirmed by permutation testing using an empiric p value <0.05

HWE: not in Hardy-Weinberg equilibrium

Yellow background: significant (p<0.05) associations in the same direction for the same phenotype in multiple racial/ethnic groups

^ Significant in meta-analysis using adjusted Bonferroni correction

F Female

M Male

Supplementary Table 4. P values for haplotype associations with renal phenotypes, adjusted for age, gender, and ancestry. Haplotypes with at least two significant ($p < 0.05$) associations are shown, along with the other haplotypes in the haplotype block. For haplotypes with a minor allele frequency $< 10\%$ the p value for the association using a dominant model is given. For haplotypes with a minor allele frequency $\geq 10\%$ the p value for the association using an additive model is given.

SNPs	frequency of haplotype	eGFR	eGFR<60	Cystatin C eGFR	Cystatin C eGFR<60	Log UAE	UAE >17/25	
ACE								
Caucasian								
Block 1	T G G A G A A G G G A	0.39	0.51	0.84	0.92	0.64	0.48	0.50
1-2-5-6-7-	A C A G A G G A A A G	0.34	0.10	0.88	0.55	0.97	0.02†	0.01†
10-11-12-14-	T G G G A G G A A A G	0.10	0.95	0.76	0.66	0.53	0.35	0.54
15-16	T G A G G G G A A A G	0.05	0.96	0.08	0.93	0.16	0.04†	0.23
	T G G G G A A G G G A	0.04	0.24	0.42	0.09	0.03†	0.04†	0.02†
	T G G A A G G A A A G	0.02	0.84	0.99	0.80	0.75	0.10	0.98
Hispanic								
Block 1	T G C G A	0.48	0.83	0.10	0.43	0.04†	0.04†	0.16
1-2-4-5-7	A C C A G	0.31	0.25	0.80	0.08	0.90	0.36	0.72
	T G C G G	0.09	0.83	0.15	0.10	0.36	0.38	0.44
	T G C A G	0.08	0.25	0.66	0.53	0.07	0.02†	0.05†
	T C C A G	0.02	0.12	0.05†	0.45	0.64	0.30	0.14
Hispanic								
Block 2	A A A G G A G	0.49	0.76	0.07	0.04†	0.80	0.04†	0.06
	G G G A A G A	0.37	0.14	0.60	0.05	0.38	0.50	0.55
	A G G A A G A	0.05	0.16	0.20	0.35	0.79	0.88	0.69
	A G G A G A G	0.02	0.78	0.55	0.72	0.79	0.73	0.25
	G G A A A G A	0.02	0.10	0.44	0.47	0.57	0.70	0.29
Hispanic								
Block 3	A A G A	0.51	0.44	0.43	0.83	0.33	0.05†	0.02†
19-20-21-22	G G G G	0.30	0.88	0.69	0.90	0.99	0.30	0.15
	G G G A	0.08	0.15	0.13	0.34	0.23	0.34	0.20
	G A G A	0.04	0.05†	0.12	0.23	0.01†	0.03†	0.02†
	A G G A	0.04	0.74	0.39	0.76	0.77	0.94	0.55
	G G A A	0.03	0.24	0.97	0.005†	0.98	0.09	0.07
AGT								
African American								
Block 2	G C A G G	0.41	0.99	0.62	0.68	0.78	0.19	0.09
4-5-6-7-8	A A G G G	0.19	0.25	0.16	0.21	0.08	0.50	0.87
	G C G A A	0.18	0.03†	0.07	0.15	0.30	0.05	0.007†
	G A G G G	0.11	0.98	0.19	0.24	0.48	0.48	0.71
	A A A G G	0.04	0.38	0.56	0.93	0.73	0.69	0.28
	G C G G G	0.03	0.45	0.23	0.88	0.85	0.24	0.69
	G C G A G	0.01	0.93	0.89	0.55	0.35	0.25	0.29
AGTR1								

African American

Block 1	G	A	G	A	A	0.53	0.19	0.01†	0.18	0.01†	0.64	0.82
1-2-3-4-5	G	A	G	G	A	0.13	0.18	0.47	0.11	0.47	0.81	0.64
	G	C	A	G	A	0.11	0.67	0.12	0.66	0.28	0.82	0.28
	G	C	A	A	A	0.08	0.65	0.71	0.69	0.53	0.49	0.27
	G	A	A	A	A	0.07	0.22	0.09	0.88	0.17	0.31	0.28
	G	C	A	G	G	0.03	0.43	0.53	0.13	0.23	0.39	0.92
	G	A	A	G	A	0.03	0.13	0.50	0.36	0.24	0.43	0.31

African American

Block 2	G	G	0.39	0.36	0.05	0.22	0.02†	0.89	0.51
6-7	A	G	0.37	0.70	0.63	0.37	0.30	0.40	0.22
	A	A	0.24	0.15	0.10	0.70	0.15	0.42	0.53

African American

Block 5	A	G	A	0.36	0.02†	0.02†	0.05	0.10	0.72	0.53
13-14-15	G	G	G	0.30	0.94	0.48	0.54	0.17	0.50	0.18
	G	G	A	0.29	0.003†	0.23	0.13	0.88	0.10	0.05
	G	A	A	0.05	0.21	0.35	0.83	0.79	0.007†	0.02†

Chinese

Block 1	A	A	G	G	A	G	G	0.50	0.47	0.67	0.88	0.08	0.90	0.33
1-2-3-4-5-6-7	A	A	G	A	A	G	G	0.30	0.36	0.32	0.87	0.03†	0.65	0.44
	A	A	G	A	A	A	A	0.07	0.73	0.17	0.69	0.57	0.52	0.95
	G	C	A	G	G	G	G	0.06	0.79	0.91	0.63	0.65	0.49	0.38
	G	A	G	G	A	G	G	0.02	0.02†	0.98	0.03†	0.98	0.84	0.89
	G	C	A	G	A	G	G	0.02	0.23	0.15	0.17	0.80	0.92	0.66

Hispanic

Block 1	A	A	G	G	A	0.50	0.03†	0.05†	0.10	0.005†	0.56	0.83
1-2-3-4-5	A	A	G	A	A	0.32	0.06	0.03†	0.23	0.002†	0.13	0.89
	G	C	A	G	G	0.09	0.37	0.67	0.27	0.59	0.01†	0.02†
	G	C	A	G	A	0.04	0.67	0.70	0.06	0.28	0.71	0.14
	G	C	A	A	A	0.03	0.18	0.71	0.71	0.37	0.48	0.25
	A	A	A	A	A	0.01	0.53	0.76	0.52	0.04†	0.88	0.89

Hispanic

Block 3	A	G	0.72	0.86	0.66	0.85	0.96	0.58	0.97
10-11	T	C	0.21	1.00	0.68	0.12	0.11	0.73	0.56
	T	G	0.07	0.94	0.93	0.02†	0.01†	0.75	0.37

AGTR2**Chinese - female**

Block 1	G	A	0.58	0.02†	0.01†	0.04†	0.17	0.31	0.28
3-6	A	G	0.40	0.03†	0.02†	0.16	0.30	0.61	0.37

Caucasian - female

Block 1	G	A	0.49	0.59	0.97	0.57	0.45	0.04†	0.07
	A	G	0.49	0.88	0.79	0.62	0.56	0.04†	0.04

Hispanic - female

Block 2	G	G	0.63	0.03†	0.01†	0.32	0.15	0.84	0.65
	G	A	0.36	0.02†	0.006†	0.30	0.13	0.59	0.66

† Association confirmed by permutation testing using an empiric p value <0.05