Supplementary materials

Common Variants in *UMOD* are associated with Urinary Uromodulin Levels:

a Meta-Analysis of 10,884 Individuals from 6 cohorts

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Supplementary Tables 1 to 5

Supplementary Table 1 . Mouse primers used in real-time RT-PCR analyses.

Gene (Protein)	Forward primer (5'-3')	Reverse primer (5'-3')	PCR Product (bp)	Efficiency
Slc38a3 (SNAT3)	GTT ATC TTC GCC CCC AAC AT	TGG GCA TGA TTC GGA AGT AG	109	0.97 ± 0.03
Slc5a2 (SGLT2)	TTG GGC ATC ACC ATG ATT TA	GCT CCC AGG TAT TTG TCG AA	164	1.02 ± 0.03
Nphs2 (Podocin)	GTC TAG CCC ATG TGT CCA AA	CCA CTT TGA TGC CCC AAA TA	162	1.03 ± 0.03
Slc12a3 (NCC)	TTT TCT GGA CCA CCA TCT CC	GTG AAG TTC CAG CCA TAG CC	148	1.01 ± 0.02
Aqp2 (AQP2)	TGA GCC TCA GAA AGG GTC TC	TCT CCA GAG CTC TCC GTC TC	142	0.98 ± 0.03
Umod (UMOD)	TTG CGA AGA ATG CAG GGT AG	TGG CAC TTT CTG AGG GAC AT	156	1.01 ± 0.02
Kcnj1 (ROMK)	CCG TGT TCA TCA CAG CCT TCT T	CCG TAA CCT ATG GTC ACT TGG G	190	1.03 ± 0.03
Sorl1 (SORL1)	CAG CCT ATC CAG GTG TAT GGA	CTA ATG CCA CGA TCA CGT TG	100	0.99 ± 0.02
Cab39 (CAB39)	GTG AGC TGC TGT TGG ACA GA	CCA CAA ACA CCT TGA ACA CG	146	1.01 ± 0.03
Gapdh (GAPDH)	TGC ACC ACC AAC TGC TTA GC	GGA TGC AGG GAT GGG GGA GA	176	1.04 ± 0.03

The primers were designed using Beacon Design 2.0 (Premier Biosoft International, Palo Alto, CA).

Supplementary Table 2: Uromodulin assay and urine samples processing.

Study	Mode of urine collection	Assay name, specifications	Lower detection limit (ng/mL)	No of unindexed uromodulin below lower detection limit	Upper detection limit (ng/mL)	No of unindexed uromodulin above upper detection limit (N)	Interval between collection and freezing (Minutes)	Temperature at which the samples were stored (ºC)	Collection of samples	No thawing before assay (N)
COLAUS	Morning urine sample	In-house UMOD ELISA	3.9	0	500	0	60-90	-80°C	2003 to 2006	None
CROATIA-Korcula	Morning urine sample	In-house UMOD ELISA	3.9	0	500	0	~30	-70C	2008 to 2010	None
CROATIA-Split	Morning urine sample	In-house UMOD ELISA	3.9	0	500	0	~30	-70C	2008 to 2010	None
FHS	Morning urine sample	Rule Based Medicine multiplex array	6.2	61	135	3	120	-80°C	1995 to 1998	Once
INGI-Carlantino	Morning urine sample	In-house UMOD ELISA	3.9	0	500	0	~5	-20°C	2005	Twice
INGI-Val Borbera	Morning urine sample	In-house UMOD ELISA	3.9	0	500	0	~120	-20°C for 1-4 weeks; then -80°C	2005 to 2008	None

Supplementary Table 3: Genotyping and imputation platforms.

Study	Array type	Genotype calling	QC filters for genotyped SNPs used for imputation	# SNPs used for imputation	Imputation	Imputation Backbone for phased CEU haplotypes (NCBI build)	Filtering of imputed genotypes	Data management and statistical analysis
COLAUS	Affymetrix 500K	BRLMM	call rate <70%, MAF <1%, pHWE <1E-7	390631	IMPUTE v0.2.0	HapMap release 21 (build 35)	none	Matlab
Croatia-KORCULA	Illumina 370CNV	GenomeStudio	HWEp<1e-6, callrate<98%, MAF<0.01	307625	MACH v1.0.16	phased CEU haplotypes, HapMap release 22 (build 36	none	GenABEL, ProbABEL
Croatia-SPLIT	Illumina 370CNV	GenomeStudio	HWEp<1e-6, callrate<98%, MAF<0.01	321456	MACH v1.0.16	phased CEU haplotypes, HapMap release 22 (build 36	none	GenABEL, ProbABEL
FHS	Affymetrix 500K mapping array and Affymetrix 50K supplemental array	Affymetrix	HWEp<1e-6, callrate<97%, Mishapp<1e-9, MAF<0.01, Mendelian errors>100, SNPs not in Hapmap or with strand issues when merging with Hapmap	378,163	MACH v1.0.15	phased CEU haplotypes, HapMap release 22 (build 36)	none	R, SAS
INGI- Carlantino	Illumina HH 370 CNV	Bead Studio	HWEp<1e-6, callrate<95%, MAF<0.01,	285,569	Mach1	phased CEU haplotypes, HapMap release 22 (build 36)	RSQ < 0.3	R GenABEL/ProbABEL
INGI-Val Borbera	Illumina SNP array 370K - HumanCNV370-Quadv3	BeadStudio	Sample Call Rate >95%, SNP Call Rate >90%, HWE P-value >10-4, MAF>0.01,	324,319	MACH v1.0.15	release 22 (build 36)	MAF < 0.01, r^2 < 0.3	R, GenABEL/ProbABEL

Supplementary Table 4: Top loci with p-values up to 1e-7 associated with raw (unindexed to urinary creatinine) urinary uromodulin in the overall population.

SNP ID	Chr	Reference allele	Non-reference allele	Effect size	p-value *	Reference allele frequency	Nearest Gene	Median Imputation Quality Across Participating Studies	eGFRcrea direction relative to reference allele	eGFRcrea p-value	R^2 to top SNP rs12917707
rs12917707	16	T	G	-0.29	1.7E-56	0.1786	*UMOD*	0.94	+	1.20E-20	same snp
rs12446492	16	A	T	-0.12	7.0E-17	0.4487	*PDILT*	0.72	+	6.90E-07	0.16
rs4238595	16	T	C	-0.11	1.7E-09	0.2906	*UMOD*	0.90	+	0.15	0.05
rs11641045	16	A	G	-0.13	3.6E-10	0.8793	*UMOD*	0.99	+	0.00048	0.03

* P-value from inverse-variance meta-analysis, corrected for genomic control. Sample size weighted meta-analysis yielded similar results.

Note: Genes nearby were based on RefSeq genes (build 36). The gene closest to the SNP is listed first and is marked bold if the SNP is located within the gene. Effects and p-values from inverse-variance meta-analysis were consistent with the sample-size weighted results.

Supplementary Table 5: VEGAS analysis for loci associated with urinary uromodulin indexed to urinary creatinine in the overall population.

Chr	Nearest Gene	nSNPs	Simulations	Start position	Stop position	Test statistic	VEGAS Pvalue	SNP	SNP-pvalue	EGFR Pvalue
16	*UMOD*	**120**	**1.00E+06**	**20251873**	**20271538**	**6827.690262**	**0**	**rs12917707**	**7.85E-73**	**1.2E-20**
16	*PDILT*	**127**	**1.00E+06**	**20277992**	**20323534**	**6852.990812**	**0**	**rs12917707**	**7.85E-73**	**1.2E-20**
16	*GP2*	**129**	**1.00E+06**	**20229311**	**20246336**	**5482.984445**	**0**	**rs12917707**	**7.85E-73**	**1.2E-20**
16	*ACSM5*	**110**	**1.00E+06**	**20328356**	**20359782**	**2827.046129**	**0**	**rs11864909**	**1.02E-41**	**1.0E-12**
8	*C8orf76*	66	1.00E+06	124301411	124322798	558.5728862	8.00E-06	rs4377946	9.46E-07	0.58
1	*TDRD5*	212	1.00E+06	177827647	177927021	1138.352998	0.000118	rs12039153	1.54E-05	0.58
8	*FAM83A*	112	1.00E+06	124263932	124291499	713.532712	0.000165	rs4377946	9.46E-07	0.58
6	*SESN1*	135	1.00E+06	109414337	109521970	1138.513874	0.000171	rs3734649	8.63E-05	0.93
8	*WDR67*	203	1.00E+06	124154100	124233571	1007.030324	0.000178	rs4377946	9.46E-07	0.25
20	*STK35*	203	1.00E+06	2031518	2077198	928.9085244	0.00047	rs6046998	0.0001195	0.19
2	*DUSP11*	48	1.00E+06	73842836	73860730	460.5605177	0.000671	rs10203740	0.0004001	0.72
1	*ATAD3C*	6	1.00E+06	1374931	1395401	48.45550841	0.000687	rs6690515	0.0001865	**0.00029**
1	*ATAD3B*	15	1.00E+06	1397026	1421445	105.386289	0.000835	rs6690515	0.0001865	**0.00029**
2	*FLJ43987*	51	1.00E+06	73864823	73897782	276.6775208	0.000854	rs10203740	0.0004001	0.00029

The table is sorted by SNP and VEGAS P-value, with significant results highlighted in bold.

Results shown for sample size weighted meta-analysis results. Inverse-variance meta-analysis yielded similar results.