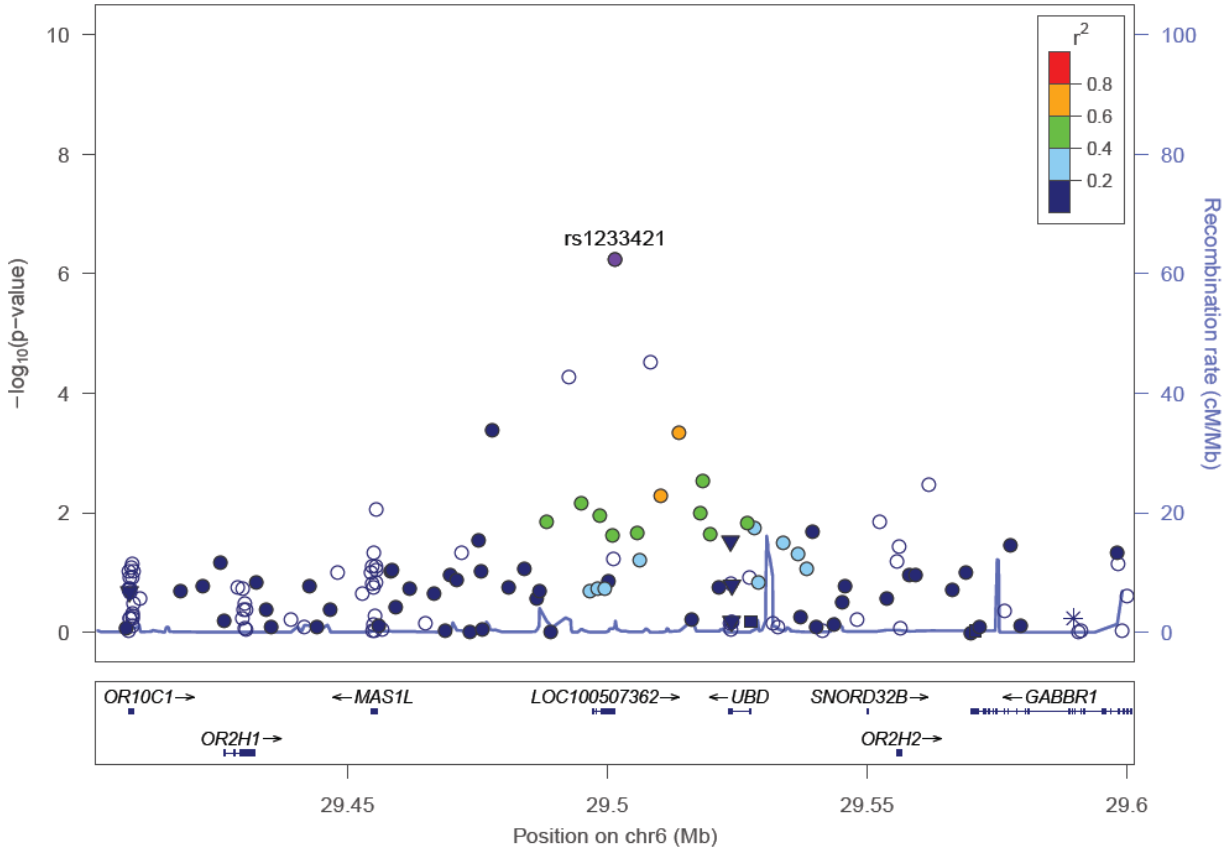
Supplementary Figure S1: Regional plot of association with plasma total ApoL1 levels at the UBD locus. Each dot represents a SNP plotted against its chromosomal position (using hg19 coordinates). The vertical axis shows -log10 p-values from single-SNP analysis for association with ApoL1 levels. The most significant SNP at the locus is shown in purple color. The remaining SNPs are color-coded according to their LD with the lead SNP as indicated by the color-key. The strength of LD is measured by pairwise R2 values based on the DHS data. Estimated recombination rates (from HapMap) are shown by the blue line, with spikes indicating locations of frequent recombination. Genes located in the region and the direction of transcription are noted below the plots based on the data from UCSC genome browser (genome.ucsc.edu). Upside triangles denote nonsynonymous variants, squares - coding variants, and filled and open circles - SNPs with no functional annotation and non-coding variants. The plot was generated using LocusZoom software.



Supplementary Table 1. Association of *APOL1* risk alleles (G1/G2) determined by MS and chronic kidney disease in DHS African Americans (n=1786)

Characteristic	0 copies (n=706)	1 copy (n=858)	2 copies (n=222)	P-value (additive model)	P-value (recessive model)
CKD, n (%)					
All (n=1676)	68 (10.0)	95 (11.5)	44 (20.2)	0.00017	<0.0001
Non-diabetic (n=1436)	38 (6.6)	54 (7.6)	37 (19.7)	<0.0001	<0.0001
Diabetic (n=240)	30 (29.4)	41 (34.7)	7 (23.3)	0.89	0.46
Microalbuminuria, n (%)					
All (n=1670)	61 (9.0	83 (10.0)	37 (17.2)	0.0012	0.00023
Non-diabetic (n=1431)	34 (5.9)	48 (6.8)	30 (16.2)	<0.0001	<0.0001
Diabetic (n=239)	27 (26.5)	35 (29.9)	7 (23.3)	0.91	0.71
GFR <60, n (%)					
All (n=1732)	17 (2.4)	23 (2.7)	15 (6.8)	0.0063	0.0012
Non-diabetic (n=1489)	12 (2.0)	12 (1.6)	14 (7.3)	0.0032	<0.0001
Diabetic (n=243)	5 (4.9)	11 (9.0)	1 (3.3)	0.78	0.45
GFR <30, n (%)	5 (0.7)	3 (0.3)	6 (2.7)	0.073	0.0031

The prevalence of CKD is compared across genotypes using logistic regression models, adjusted for age, gender, systolic BP and diabetes, where appropriate.
Microalbuminuria - urine albumin/creatinine ratio (ACR) ≥17 mg/g in men or ≥25 mg/g in women. GFR - glomerular filtration rate. CKD - chronic kidney disease; defined as the presence of microalbuminuria and/or GFR <60 ml/min/1.73 m^2.

Supplementary Table 2. Association between circulating APOL1 levels and chronic kidney disease in DHS African Americans

Outcome	APOL1 protein	N subjects	Model 1		Model 2	
			OR (95% CI)	P-value	OR (95% CI)	P-value
CKD	Total APOL1	1729	0.97 (0.83-1.14)	0.75	1.00 (0.86-1.17)	0.97
	WT APOL1	1453	1.00 (0.83-1.19)	0.96	1.11 (0.87-1.42)	0.39
	G1 APOL1	686	1.22 (0.99-1.50)	0.063	1.18 (0.92-1.52)	0.2
	G2 APOL1	463	1.23 (0.94-1.62)	0.13	1.28 (0.93-1.75)	0.13
	G1+G2 APOL1	1038	1.32 (1.11-1.57)	0.0014	1.16 (0.93-1.44)	0.19
Microalbuminuria	Total APOL1	1723	0.95 (0.81-1.13)	0.58	0.98 (0.82-1.16)	0.78
	WT APOL1	1450	0.98 (0.81-1.2)	0.88	1.07 (0.83-1.39)	0.6
	G1 APOL1	681	1.2 (0.97-1.5)	0.099	1.15 (0.88-1.51)	0.31
	G2 APOL1	461	1.12 (0.83-1.51)	0.46	1.14 (0.82-1.6)	0.44
	G1+G2 APOL1	1032	1.26 (1.05-1.52)	0.012	1.1 (0.87-1.39)	0.43
GFR <60	Total APOL1	1788	0.79 (0.59-1.07)	0.13	0.82 (0.61-1.11)	0.21
	WT APOL1	1504	0.95 (0.68-1.33)	0.76	1.01 (0.65-1.57)	0.96
	G1 APOL1	702	1.01 (0.67-1.52)	0.95	0.92 (0.58-1.47)	0.73
	G2 APOL1	478	1.57 (1.04-2.36)	0.03	1.86 (1.08-3.2)	0.025
	G1+G2 APOL1	1069	1.34 (1.02-1.78)	0.038	1.06 (0.73-1.55)	0.75

The analysis includes all DHS African American participants with available data on microalbuminuria, GFR and total CKD. The analysis of allele-specific protein levels is restricted to individuals who carry at least one copy of the corresponding allele. For example, the analysis of wild-type APOL1 levels is confined to individuals with 0 or 1 copies of the G1 and G2 alleles. The analysis of total levels of the variant protein (G1 + G2 APOL1) is restricted to individuals with at least 1 copy of the variant alleles (G1 or G2). Model 1 includes age, gender, systolic BP and diabetes as covariates. Model 2 is additionally adjusted for the number of copies of the risk alleles. Odds ratios (OR) are calculated per 1 SD increase in circulating APOL1 levels. N subjects – number of individuals included in each analysis; 95% CI – 95% confidence interval.

Supplementary Table 3. Association between circulating ApoL1 levels and chronic kidney disease in DHS African Americans stratified by the number of *APOL1* risk alleles

	APOL1		1 risk allele			2 risk alleles	
Oucome	**protein**	**N**	**OR (95% CI)**	**P**	**N**	**OR (95% CI)**	**P**
CKD	Total APOL1	811	0.97 (0.76-1.23)	0.79	226	1.04 (0.73-1.49)	0.82
	WT APOL1	811	1.07 (0.76-1.51)	0.71	-	-	-
	G1 APOL1	602	1.21 (0.86-1.71)	0.28	83	1.32 (0.89-1.94)	0.16
	G2 APOL1	424	1.10 (0.74-1.64)	0.63	38	1.44 (0.82-2.53)	0.2
	G1+G2 APOL1	811	1.10 (0.76-1.58)	0.61	226	1.29 (0.98-1.70)	0.065
Microalbuminuria	Total APOL1	808	0.96 (0.74-1.24)	0.75	223	0.96 (0.65-1.43)	0.86
	WT APOL1	808	1.04 (0.72-1.51)	0.83	-	-	-
	G1 APOL1	598	1.10 (0.76-1.61)	0.61	82	1.39 (0.92-2.10)	0.12
	G2 APOL1	423	0.92 (0.6-1.41)	0.7	37	1.29 (0.72-2.29)	0.39
	G1+G2 APOL1	808	1.04 (0.7-1.54)	0.84	223	1.22 (0.92-1.64)	0.17
GFR <60	Total APOL1	837	0.95 (0.62-1.46)	0.81	231	0.79 (0.42-1.47)	0.45
	WT APOL1	837	1.13 (0.64-2.00)	0.68	-	-	-
	G1 APOL1	617	1.19 (0.66-2.15)	0.56	84	0.62 (0.23-1.64)	0.34
	G2 APOL1	435	1.83 (0.94-3.54)	0.074	42	4.48 (0.43-46.69)	0.21
	G1+G2 APOL1	837	1.33 (0.69-2.54)	0.39	231	1.09 (0.68-1.76)	0.71

The analysis includes all DHS African American participants with available data on microalbuminuria, GFR and total CKD. The analysis of allele-specific protein levels is restricted to individuals who carry at least one copy of the corresponding allele. For example, the analysis of wild-type APOL1 levels is confined to individuals with 0 or 1 copies of the G1 and G2 alleles. The analysis of total levels of the variant protein (G1 + G2 APOL1) is restricted to individuals with at least 1 copy of the variant alleles (G1 or G2). Odds ratios (OR) are calculated per 1 SD increase in circulating APOL1 levels. N – number of individuals included in each analysis; 95% CI – 95% confidence interval.

Supplementary Table 4. Variants associated with plasma total APOL1 levels in exome-wide analysis in DHS (n=3354)

SNP	Chr.	Position	Gene	AA change	EA	EAF (%)			BETA (s.d. units)	P-value (single-SNP)	P-value (conditional on rs35370634)	P-value (joint analysis)
						AFR	EUR	HIS				
rs1233421	6	29501514			A	53.2	47.1	43.8	0.11	4.90E-07	2.51E-06	1.42E-06
rs7197514	16	65652630			G	63.9	1.9	8.2	0.16	5.45E-08	3.30E-07	
rs1110471	16	66350593			A	15.7	84.9	78.6	-0.20	1.91E-11	7.53E-10	
rs9928279	16	66527099	BEAN1	K128E	G	22.5	0.3	2.9	0.17	3.11E-07	1.64E-06	
rs9932319	16	67131601	CBFB		G	72.1	8.0	14.1	0.15	4.65E-08	1.38E-06	
rs12923138	16	67233266	ELMO3	K66Q	A	10.3	57.5	54.7	-0.15	2.31E-08	5.43E-08	
rs8044843	16	67318242	PLEKHG4	D525G	G	64.7	11.7	15.5	0.14	4.26E-08	1.23E-07	
rs3868142	16	67320223	PLEKHG4	R830H	A	58.2	8.6	10.6	0.16	6.67E-10	6.11E-09	
rs9922085	16	67397580	LRRC36	R222P	G	52.8	5.0	9.5	0.17	1.04E-10	1.55E-09	
rs8052655	16	67409180	LRRC36	G509S	A	52.8	5.0	9.5	0.17	9.61E-11	1.48E-09	2.66E-07
rs6979	16	67691668	ACD	V518A	A	9.5	50.1	52.4	-0.14	2.17E-07	2.37E-07	
rs1424114	16	69224615	SNTB2		G	15.0	63.3	68.1	-0.15	1.26E-08	5.04E-08	
rs11537667	16	70303659	AARS	G275D	A	24.6	0.3	2.9	0.18	9.13E-08	8.55E-07	
rs7195567	16	70351429	DDX19B		C	24.6	0.3	3.1	0.19	3.79E-08	4.31E-07	
rs76351450	16	71317533	FTSJD1	N764S	G	14.7	0.1	2.1	0.25	4.96E-10	1.53E-08	
rs61733124	16	71682830	PHLPP2	R1312Q	A	9.8	8.5	8.0	0.21	1.57E-08	6.62E-07	2.91E-07
rs61733127	16	71683718	PHLPP2	L1016S	G	4.0	16.1	6.5	-0.23	5.13E-09	0.028	
rs1559401	16	72011181	PKD1L3	H571Q	C	25.5	23.3	41.9	0.16	1.12E-11	5.88E-08	
rs7185272	16	72013797	PKD1L3	T429S	G	25.5	23.2	41.9	0.16	1.08E-11	5.78E-08	
rs72787027	16	72033801	PKD1L3	P26Q	A	2.7	20.2	7.0	-0.27	3.25E-12	0.36	
rs2000999	16	72108093	HPR		A	7.0	18.8	16.7	-0.23	1.57E-13	3.84E-14	7.38E-12
rs34832584	16	72162966	PMFBP1	T505K	A	2.4	16.4	6.2	-0.33	4.05E-16	0.87	
rs35370634	16	72184566	PMFBP1	E48K	A	2.5	16.4	6.2	-0.33	2.10E-16	-	1.41E-13
rs16970661	16	72218612			A	30.7	0.4	4.7	0.20	1.40E-10	4.21E-10	9.87E-10
rs60664312	16	75657221	ADAT1		A	38.9	4.4	6.5	0.16	6.50E-09	6.27E-08	
rs7201030	16	76523792	CNTNAP4		G	16.6	87.9	71.6	-0.15	1.10E-07	3.52E-07	
rs41297245	22	36657740	APOL1	G96R	A	4.7	6.2	2.3	-0.25	4.18E-07	1.20E-07	5.75E-08

AA - amino acid; EA - effect allele; EAF - effect allele frequency; AFR - African American; EUR - European American; HIS - Hispanic. Chromosome positions are given for hg19. The AA change column shows the predicted change in amino acid sequence. Effects are reported for the less common allele in the combined DHS population.

Supplementary Table 5. Association of top variants identified in exome-wide analysis with CKD phenotypes

					ACR		GFR		CKD		Micro-albuminuria		GFR < 60	
SNP	Chr.	Gene	EA	EAF (%)	Beta	P-value	Beta	P-value	OR	P-value	OR	P-value	OR	P-value
DHS combined														
rs1233421	6		A	49.1	0.02	0.415	-0.03	0.186	1.17	0.089	1.19	0.084	1.04	0.813
rs8052655	16	*LRRC36*	A	30.6	-0.01	0.673	0.01	0.797	1.02	0.843	1.02	0.874	0.95	0.798
rs61733124	16	*PHLPP2*	A	8.9	0.00	0.977	-0.01	0.708	0.98	0.891	1.03	0.876	0.76	0.365
rs2000999	16	*HPR*	A	13.2	0.07	0.064	-0.05	0.157	1.23	0.126	1.13	0.422	1.86	**0.0060**
rs35370634	16	*PMFBP1*	A	7.7	-0.04	0.449	0.04	0.406	0.89	0.573	0.88	0.561	1.09	0.791
rs16970661	16		A	16.6	-0.01	0.863	0.03	0.374	0.87	0.239	0.87	0.279	1.24	0.324
rs41297245	22	*APOL1*	A	4.7	-0.07	0.214	0.04	0.456	0.59	0.046	0.62	0.092	0.25	0.053
African American														
rs1233421	6		A	53.5	0.02	0.640	-0.03	0.289	1.14	0.260	1.09	0.485	1.28	0.244
rs8052655	16	*LRRC36*	A	53.3	0.00	0.941	0.02	0.460	1.09	0.419	1.09	0.441	1.02	0.941
rs61733124	16	*PHLPP2*	A	9.9	0.00	0.985	-0.01	0.914	1.14	0.446	1.13	0.521	0.96	0.896
rs2000999	16	*HPR*	A	6.9	0.07	0.297	-0.07	0.282	1.36	0.137	1.10	0.686	2.29	**0.0080**
rs35370634	16	*PMFBP1*	A	2.7	-0.06	0.563	0.09	0.348	0.99	0.974	0.86	0.703	0.77	0.721
rs16970661	16		A	30.7	0.01	0.807	0.04	0.297	0.88	0.294	0.89	0.359	1.23	0.347
rs41297245	22	*APOL1*	A	4.8	-0.14	0.076	0.04	0.632	0.60	0.119	0.70	0.281	0.00	0.984
European American														
rs1233421	6		A	46.5	0.02	0.663	0.00	0.944	1.20	0.424	1.43	0.179	0.72	0.376
rs8052655	16	*LRRC36*	A	4.7	-0.10	0.372	-0.01	0.945	0.41	0.225	0.00	0.988	0.97	0.973
rs61733124	16	*PHLPP2*	A	8.0	-0.02	0.789	0.03	0.710	0.63	0.329	0.92	0.862	0.31	0.255
rs2000999	16	*HPR*	A	20.2	0.12	**0.027**	-0.03	0.575	1.18	0.514	1.33	0.323	1.44	0.332
rs35370634	16	*PMFBP1*	A	16.7	-0.06	0.338	0.03	0.584	0.80	0.470	1.06	0.865	0.97	0.949
rs16970661	16		A	0.2	-0.56	0.272	0.41	0.403	0.00	0.991	0.00	0.991	0.00	0.995
rs41297245	22	*APOL1*	A	6.2	0.08	0.400	0.11	0.199	0.66	0.416	0.72	0.574	0.36	0.312
Hispanic American														

rs1233421	6		A	43.3	0.01	0.848	-0.08	0.137	1.41	0.167	1.49	0.112	0.20	0.209
rs8052655	16	*LRRC36*	A	9.2	-0.21	0.061	-0.11	0.260	0.49	0.220	0.51	0.250	0.00	0.995
rs61733124	16	*PHLPP2*	A	7.6	0.08	0.450	-0.08	0.409	0.56	0.265	0.57	0.291	0.00	0.995
rs2000999	16	*HPR*	A	17.6	-0.06	0.435	-0.06	0.416	1.14	0.672	1.08	0.802	2.03	0.440
rs35370634	16	*PMFBP1*	A	6.8	0.09	0.455	0.11	0.310	0.50	0.257	0.53	0.299	0.00	0.996
rs16970661	16		A	4.3	-0.23	0.132	-0.06	0.678	0.58	0.461	0.60	0.481	0.00	0.996
rs41297245	22	*APOL1*	A	2.5	-0.11	0.575	-0.15	0.381	0.53	0.541	0.00	0.984	3.70	0.231

EA - effect allele; EAF - effect allele frequency; OR - odds ratio; ACR - urine albumin/creatinine ratio; GFR - glomerular filtration rate. Microalbuminuria - ACR ≥17 mg/g in men or ≥25 mg/g in women. CKD - chronic kidney disease; defined as the presence of microalbuminuria and/or GFR <60 ml/min/1.73 m^2. Effects sizes (Beta) are given in s.d. units. Nominally significant p-values are shown in bold face.

Supplementary Table 6: Cox proportional hazards regression analysis of time to CVD event in African American participants of DHS

Factor	Number of Subjects	Number of CVD Events	Hazard Ratio (95% CI)	P-value
Total APOL1 (nM)	1379	137	1.000 (1.000 - 1.001)	0.56
WT APOL1 (nM)	1159	112	1.001 (1.000 - 1.002)	0.27
G1 APOL1 (nM)	540	60	1.000 (0.999 - 1.002)	0.65
G2 APOL1 (nM)	385	40	1.001 (0.998 - 1.003)	0.52
G1 + G2 APOL1 (nM)	840	86	1.000 (0.999 - 1.001)	0.93
APOL1 genotypes (2 risk alleles vs 0-1 risk alleles)	1340	134	1.124 (0.710 – 1.778)	0.62

The end point was total cardiovascular disease outcome, defined as a first nonfatal myocardial infarction, nonfatal stroke, coronary revascularization (percutaneous coronary intervention or coronary-artery bypass grafting), peripheral revascularization, hospitalization for heart failure or atrial fibrillation, or death from cardiovascular causes. All end points were adjudicated by two cardiologists. The National Death Index was used to determine vital status for all the participants through December 31, 2010. Death from cardiovascular causes was defined according to the *International Classification of Diseases, 10th Revision,* codes I00 to I99. Individuals with a history of cardiovascular disease (self-reported history of myocardial infarction, stroke, arterial revascularization, heart failure, or arrhythmia) and persons who died within 1 year after enrollment were excluded. The median follow-up period was 9.3 years.