SUPPLEMENTAL FILE

Apolipoprotein L1 plasma levels do not correlate with chronic kidney disease.

Supplemental Table 1: Comparison of *APOL1* allele frequency with published studies (all African American).

Cohort description	HIV status	CKD case/control	G0	G1*	G2	# Subjects	Reference
Nephrotic range proteinuria	positive	case	0.67	0.18	0.15	39	this study
Nephrotic range proteinuria	positive	matched control	0.68	0.22	0.10	88	this study
eGFR<60ml/min	positive	case	0.53	0.31	0.16	44	this study
eGFR<60ml/min	positive	matched control	0.69	0.19	0.12	91	this study
Non-HIVAN CKD	positive	case	0.48	0.31	0.21	98	1
HIVAN	positive	case	0.18	0.54	0.28	54	2
Normal	positive	control	0.67	0.20	0.13	237	2
FSGS	negative	case	0.20	0.55	0.25	217	2
Normal	negative	control	0.64	0.23	0.13	383	2
FSGS (Brigham cohort)		case	0.13	0.68	0.19	52	3
FSGS (NIH cohort)		case	0.28	0.47	0.25	140	3
Hypertensive end stage CKD		case	0.38	0.41	0.21	1002	3
Combined normals		control	0.66	0.21	0.13	1099	3
IgA Nephropathy		case	0.59	0.21	0.20	35	4
FSGS		case	0.25	0.50	0.25	44	4
HIVAN	positive	case	0.29	0.46	0.25	21	4
Normal		control	0.60	0.26	0.14	74	4
Hypertensive CKD (AASK)		case	0.56	0.28	0.16	675	5
Normal (Wake Forest cohort)		control	0.66	0.21	0.13	618	5
Dallas Heart Study		general population	0.62	0.23	0.15	1825	6
Atherosclerosis Risk in Communities		general population	0.65	0.22	0.13	3067	7

*Where the 2 SNPs comprising the G1 haplotype are reported separately the variant rs73885319 is used for the G1 frequency.

Reference List for Supplemental Table 1.

1. Fine DM, Wasser WG, Estrella MM, Atta MG, Kuperman M, Shemer R, Rajasekaran A, Tzur S, Racusen LC, Skorecki K: APOL1 risk variants predict histopathology and progression to ESRD in HIV-related kidney disease. *J Am Soc Nephrol* 23:343-350, 2012

2. Kopp JB, Nelson GW, Sampath K, Johnson RC, Genovese G, An P, Friedman D, Briggs W, Dart R, Korbet S, Mokrzycki MH, Kimmel PL, Limou S, Ahuja TS, Berns JS, Fryc J, Simon EE, Smith MC, Trachtman H, Michel DM, Schelling JR, Vlahov D, Pollak M, Winkler CA: APOL1 genetic variants in focal segmental glomerulosclerosis and HIV-associated nephropathy. *J Am Soc Nephrol* 22:2129-2137, 2011

3. Genovese G, Friedman DJ, Ross MD, Lecordier L, Uzureau P, Freedman BI, Bowden DW, Langefeld CD, Oleksyk TK, Uscinski Knob AL, Bernhardy AJ, Hicks PJ, Nelson GW, Vanhollebeke B, Winkler CA, Kopp JB, Pays E, Pollak MR: Association of trypanolytic ApoL1 variants with kidney disease in African Americans. *Science* 329:841-845, 2010

4. Papeta N, Kiryluk K, Patel A, Sterken R, Kacak N, Snyder HJ, Imus PH, Mhatre AN, Lawani AK, Julian BA, Wyatt RJ, Novak J, Wyatt CM, Ross MJ, Winston JA, Klotman ME, Cohen DJ, Appel GB, D'Agati VD, Klotman PE, Gharavi AG: APOL1 variants increase risk for FSGS and HIVAN but not IgA nephropathy. *J Am Soc Nephrol* 22:1991-1996, 2011

5. Lipkowitz MS, Freedman BI, Langefeld CD, Comeau ME, Bowden DW, Kao WH, Astor BC, Bottinger EP, Iyengar SK, Klotman PE, Freedman RG, Zhang W, Parekh RS, Choi MJ, Nelson GW, Winkler CA, Kopp JB: Apolipoprotein L1 gene variants associate with hypertension-attributed nephropathy and the rate of kidney function decline in African Americans. *Kidney Int* 83:114-120, 2013

6. Friedman DJ, Kozlitina J, Genovese G, Jog P, Pollak MR: Population-based risk assessment of APOL1 on renal disease. *J Am Soc Nephrol* 22:2098-2105, 2011

7. Foster MC, Coresh J, Fornage M, Astor BC, Grams M, Franceschini N, Boerwinkle E, Parekh RS, Kao WH: APOL1 Variants Associate with Increased Risk of CKD among African Americans. *J Am Soc Nephrol* 24:1484-1491, 2013.

Supplemental Table 2: *APOL1* risk allele genotype and allele frequency in CKD and control groups **excluding diabetics***.

		n (%) Genotype				Allele Frequency		
		0 risk alleles	1 risk allele	2 risk alleles		G0	G1	G2
eGFR<60ml/min cohort	Cases (n=37)	8 (22)	22 (59)	7 (19)		0.52	0.32	0.16
	Controls (n=81)	37 (46)	39 (48)	5 (6)		0.70	0.17	0.13
Nephrotic proteinuria cohort	Cases (n=32)	15 (47)	14 (44)	3 (9)		0.69	0.17	0.14
	Controls (n=87)	42 (48)	34 (39)	11 (13)		0.68	0.22	0.10

*Total of 27 diabetics, two were not genotyped.

Supplemental Table 3: Dependence of *APOL1* genotype on plasma levels of APOL1 and inflammatory mediators.

	All Controls				All Cases			
	0 risk alleles (n=82)	**1 risk allele (n=80)**	**2 risk alleles (n=16)**		**0 risk alleles (n=26)**	**1 risk allele (n=46)**	**2 risk alleles (n=10)**	
Variable	**median**	**median**	**median**	***P***	**median**	**median**	**median**	***P***
APOL1	3107.2	3071.3	2792.2	0.51	3882.1	4234.4	2860.9	0.75
C reactive protein	1790.0	1868.5	1066.0	0.37	2979.5	2494.0	2552.0	0.29
β2-microglobulin	988.0	1078.5	836.5	0.31	1436.0	1404.0	2536.5	0.36
sTNFR1	2668.0	2598.0	2293.0	0.67	3525.0	3835.0	4125.5	0.35
sTNFR2	5047.0	5080.0	3645.0	0.23	6776.0	8417.0	12829.5	0.24
Interleukin-6	4.7	4.7	4.5	0.99	7.0	7.1	6.1	0.64
CCL2	202.0	234.0	185.5	0.63	284.0	288.0	327.5	0.09
CCL5	33227.0	24456.5	24272.0	0.05	45317.5	24222.0	42156.0	0.09
Interferon-α	2.0	2.0	1.5	0.57	2.3	2.6	2.6	0.04

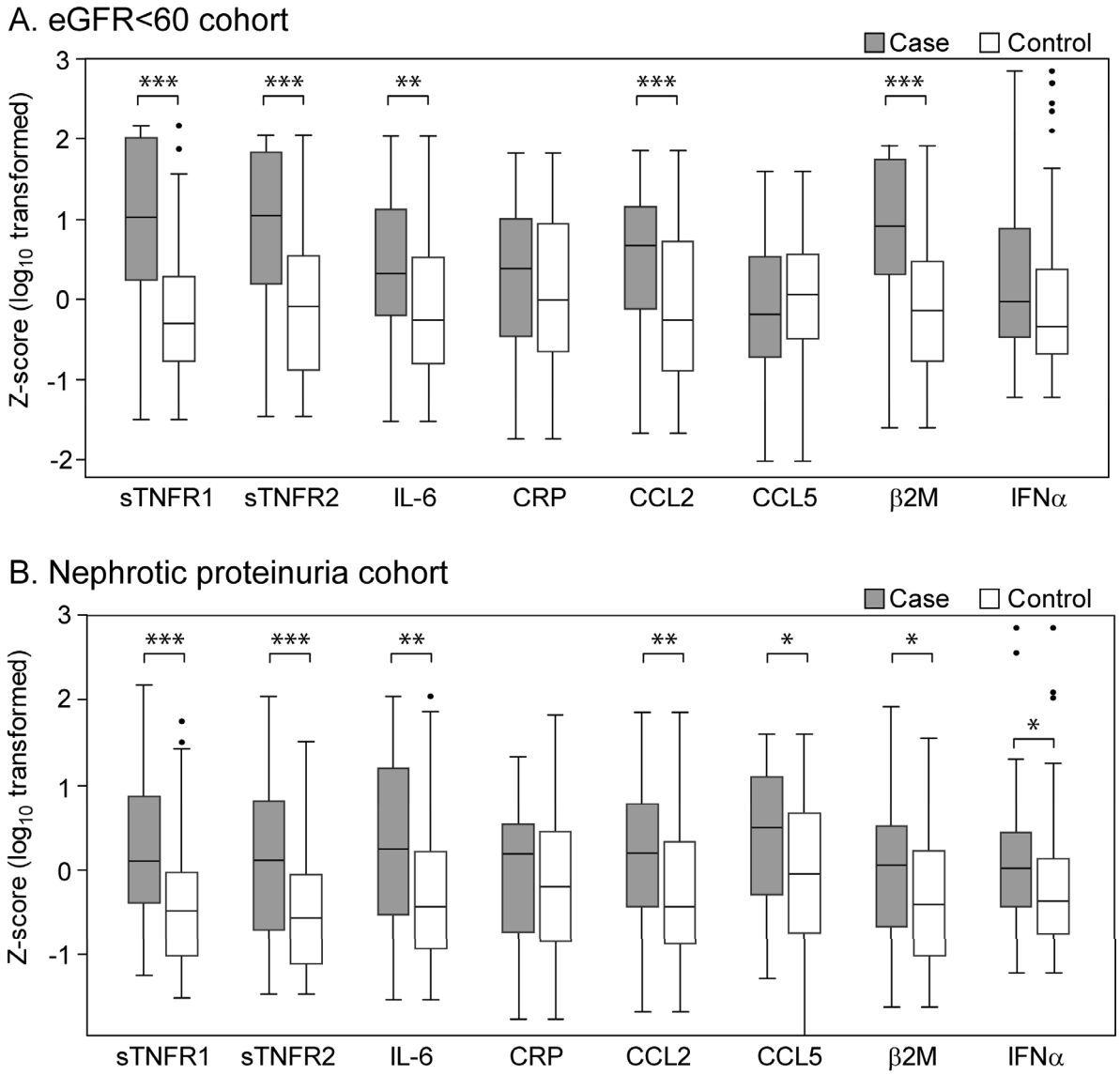
All values in pg/ml, except APOL1 and C reactive protein in ng/ml and β2-microglobulin in μg/ml.

Supplemental Table 4: Univariate and multivariate conditional logistic regression for CKD in eGFR<60ml/min cohort.

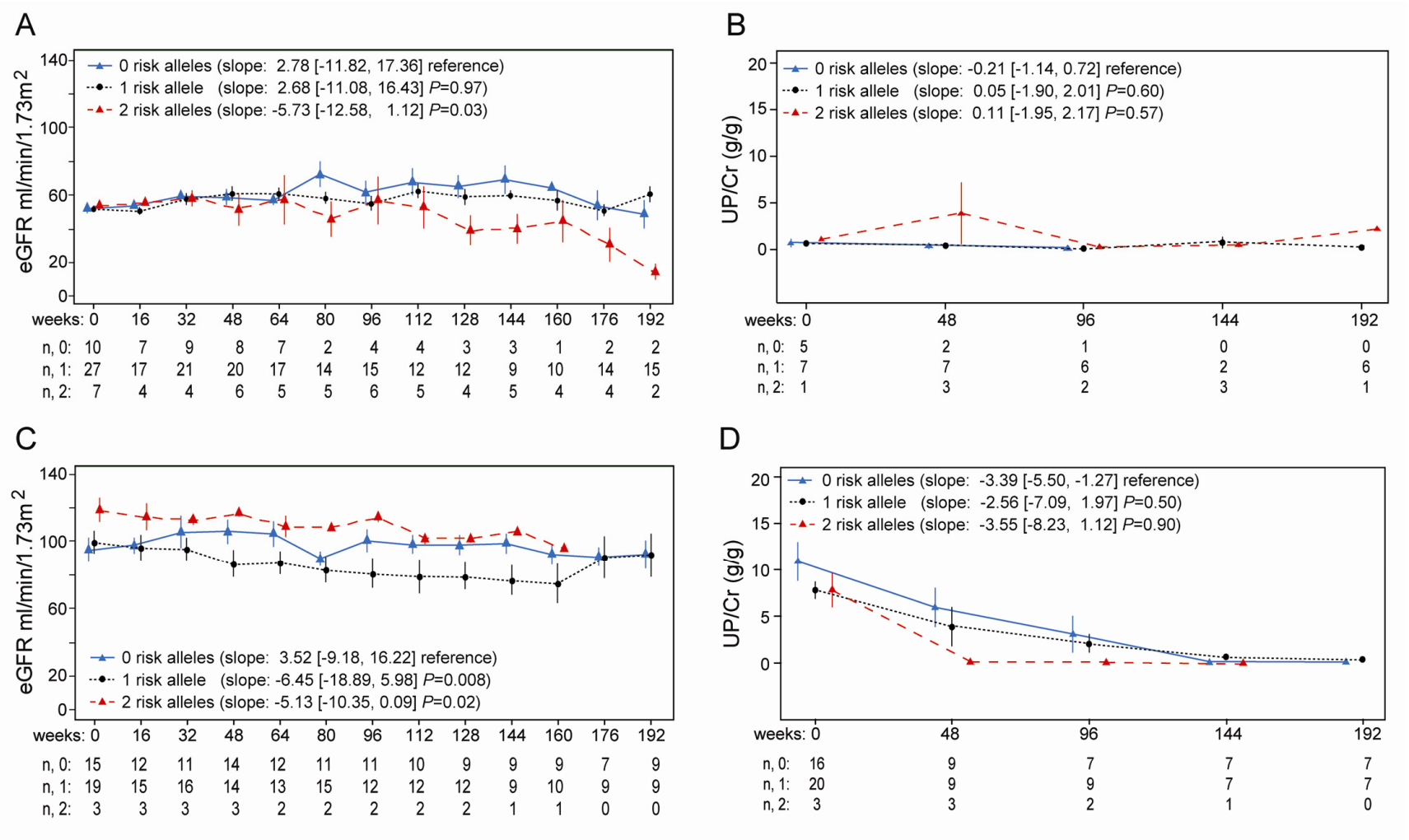
	Univariate	**Multivariate Model 1 (n=135)**	**Multivariate Model 2 (n=135)**			
	OR (95% CI) ***P***	**OR (95% CI)** ***P***	**OR (95% CI)** ***P***	**OR (95% CI)** ***P***	**OR (95% CI)** ***P***	**OR (95% CI)** ***P***
1 *APOL1* risk allele *vs. 0 risk alleles*	2.80 (1.13, 6.95) <0.01	5.13 (1.49, 17.65) <0.01	5.43 (1.18, 24.93) <0.05	4.45 (1.02, 19.33) <0.05	6.48 (1.51, 27.68) <0.05	7.32 (1.72, 31.18) <0.01
2 *APOL1* risk alleles *vs. 0 risk alleles*	6.18 (1.55, 24.59) <0.01	18.25 (2.36, 141.27) <0.01	9.74 (0.83, 113.72) NS	15.64 (1.46, 167.15) <0.01	19.12 (1.51, 241.28) <0.001	28.81 (2.62, 317.08) <0.01
Age *per year*	1.13 (1.07, 1.19) <0.001					
Sex *Women vs. Men*	2.78 (1.31, 5.90) <0.01					
Hypertension	6.50 (2.44, 17.35) <0.001	8.21 (2.52, 26.82) <0.001	4.91 (1.24, 19.37) <0.05	3.93 (0.93, 16.48) NS	5.03 (1.10, 23.04) <0.05	6.75 (1.81, 25.23) <0.01
Diabetes	1.52 (0.51, 4.49) NS					
Hepatitis C	2.04 (0.90, 4.62) NS	3.28 (1.04, 10.35) <0.05	2.75 (0.62, 12.22) NS	2.39 (0.62, 9.18) NS	2.12 (0.59, 7.66) NS	2.29 (0.65, 7.98) NS
Fasting Cholesterol	1.67 (0.96, 2.91) NS					
TDF exposure	1.73 (0.78, 3.81) NS	3.52 (1.10, 111.35) <0.05	2.10 (0.51, 8.67) NS	3.35 (0.83, 13.51) NS	3.344 (0.81, 14.62) NS	3.68(1.00, 13.63) <0.05
sTNFR1 *per 1 s.d. increase*	3.40 (2.05, 5.65) <0.001		3.04 (1.58, 5.84) <0.001			
sTNFR2 *per 1 s.d. increase*	3.75 (2.08, 6.76) <0.001			2.99 (1.49, 6.02) <0.001		
β2 Microglobulin *per 1 s.d. increase*	3.63 (2.08, 6.33) <0.001				3.42 (1.63, 7.18) <0.001	
CCL2 *per 1 s.d. increase*	2.37 (1.48, 3.79) <0.001					2.23 (1.28, 3.90) <0.01
IL6 *per 1 s.d. increase*	1.87 (1.22, 2.86) <0.01					
CRP *per 1 s.d. increase*	1.25 (0.87, 1.80) NS					
CCL5 *per 1 s.d. increase*	0.85 (0.33, 2.21) NS					
Interferon-α *per 1 s.d. increase*	2.06 (0.57, 7.42) NS					

Supplemental Table 5: Univariate and multivariate conditional logistic regression for CKD in nephrotic proteinuria cohort.

	Univariate	**Multivariate Model 1 (n=132)**	**Multivariate Model 2 (n=132)**			
	OR (95% CI) ***P***	**OR (95% CI)** ***P***	**OR (95% CI)** ***P***	**OR (95% CI)** ***P***	**OR (95% CI)** ***P***	**OR (95% CI)** ***P***
1 *APOL1* risk allele *vs. 0 risk alleles*	1.89 (0.75, 4.77) NS					
2 *APOL1 risk* alleles *vs. 0 risk alleles*	0.68 (0.17, 2.63) NS					
Age *per year*	1.04 (1.00, 1.08) NS					
Sex *Women vs. Men*	1.85 (0.67, 5.08) NS					
Hypertension	3.39 (1.39, 8.25) <0.01	3.49 (1.32, 9.24) <0.05	2.76 (0.97, 7.85) NS	3.50 (1.25, 9.78) <0.05	3.57 (1.25, 10.14) <0.05	3.77 (1.33, 10.71) <0.05
Diabetes	*P*<0.001 (see text)					
Hepatitis C	5.75 (1.56, 21.20) <0.01	6.11 (1.48, 25.27) <0.05	4.70 (1.04, 21.24) <0.05	3.18 (0.68, 14.90) NS	5.96 (1.33, 26.80) <0.05	4.55 (0.99, 20.98) NS
Fasting Cholesterol	1.29 (0.83, 2.01) NS					
TDF exposure	1.11 (0.52, 2.36) NS					
sTNFR1 *per 1 s.d. increase*	2.31 (1.46, 3.66) <0.001		2.02 (1.23, 3.25) <0.01			
sTNFR2 *per 1 s.d. increase*	2.53 (1.51, 4.26) <0.001			2.26 (1.23, 4.13) <0.01		
β2 Microglobulin *per 1 s.d. increase*	2.01 (1.17, 3.44) <0.05					
CCL2 *per 1 s.d. increase*	1.93 (1.24, 3.00) <0.01					1.75 (1.08, 2.83) <0.05
IL6 *per 1 s.d. increase*	1.74 (1.20, 2.54) <0.01				1.66 (1.02, 2.51) <0.05	
CRP *per 1 s.d. increase*	1.07 (0.74, 1.56) NS					
CCL5 *per 1 s.d. increase*	1.52 (1.06, 2.18) <0.05					
Interferon-α *per 1 s.d. increase*	1.82 (1.08, 3.07) NS					



Supplemental Figure 1. Box whisker plots of cytokine plasma levels comparing CKD cases and controls. A. eGFR<60ml/min cohort. B. Nephrotic proteinuria cohort. Data was $\log_{10}$ transformed and Z-scores (value of each variable subtracted from their mean and then divided by their standard deviation) were used to allow comparisons between cytokines. Boxes denote interquartile range with a median line, filled circles represent outliers from the range whiskers. *$0.05<P>0.01$; **$0.01\leq P\geq 0.001$; ***$P<0.001$ by univariate regression model, where outliers were Winsorised to the 95th percentile (see Supplemental Table 4 and 5 for odds ratios for CKD).



Supplemental Figure 2. Longitudinal changes in renal function in cases by number of *APOL1* risk alleles. A, B. Changes in (A) eGFR and (B) urinary protein to creatinine ratios (UP/Cr) for the cases in the eGFR<60 cohort. C, D. Changes in (C) eGFR and (D) UP/Cr for the cases in the nephrotic range proteinuria cohort. Controls in both cohorts did not change over time (see matching criteria in methods). Graphical data are time point means with standard error bars. Slopes were determined for each participant and are presented in the legend as a mean slope in ml/min/year for eGFR or g/g/year for proteinuria [interquartile range] and probability (*P*) values versus 0 risk alleles. Below each graph are the numbers of participants (n) with available data for 0, 1, or 2 risk alleles per each time point.