Supplementary Table 1. rs667704 is associated with eQTLS for *CFHR1* and *CFHR3* within diverse human tissues (GTEx, reference 8)

Gencode Id	Gene	SNP Id	P-Value	Effect Size	Tissue
ENSG00000116785.9	CFHR3	rs6677604	2.50E-19	-0.72	Thyroid
ENSG00000116785.9	CFHR3	rs6677604	3.00E-18	-0.73	Lung
ENSG00000244414.2	CFHR1	rs6677604	4.50E-16	-0.97	Liver
ENSG00000116785.9	CFHR3	rs6677604	3.00E-14	-0.96	Liver
ENSG00000116785.9	CFHR3	rs6677604	5.10E-13	-0.9	Adrenal Gland
ENSG00000116785.9	CFHR3	rs6677604	1.30E-12	-0.58	Nerve - Tibial
ENSG00000116785.9	CFHR3	rs6677604	2.20E-11	-0.64	Esophagus - Muscularis
ENSG00000116785.9	CFHR3	rs6677604	5.00E-11	-0.68	Artery - Aorta
ENSG00000116785.9	CFHR3	rs6677604	1.10E-10	-0.71	Colon - Transverse
ENSG00000116785.9	CFHR3	rs6677604	6.70E-09	-0.61	Esophagus - Mucosa
ENSG00000116785.9	CFHR3	rs6677604	2.60E-08	-0.67	Prostate
ENSG00000116785.9	CFHR3	rs6677604	2.40E-07	-0.67	Stomach
ENSG00000116785.9	CFHR3	rs6677604	4.40E-07	-0.68	Adipose - Visceral (Omentum)
ENSG00000244414.2	CFHR1	rs6677604	9.20E-07	-0.29	Cells - Transformed fibroblasts
ENSG00000244414.2	CFHR1	rs6677604	0.0000016	-0.74	Spleen
ENSG00000116785.9	CFHR3	rs6677604	0.0000016	-0.45	Breast - Mammary Tissue
ENSG00000116785.9	CFHR3	rs6677604	0.0000019	-0.64	Artery - Coronary
ENSG00000116785.9	CFHR3	rs6677604	0.0000021	-0.52	Heart - Atrial Appendage
ENSG00000116785.9	CFHR3	rs6677604	0.0000029	-0.72	Spleen
ENSG00000177888.7	ZBTB41	rs6677604	0.000013	-0.2	Adipose - Subcutaneous
ENSG00000244414.2	CFHR1	rs6677604	0.000021	-0.33	Nerve - Tibial

Supplementary Table 2. Study Cohorts

		SNP genotyped (post-QC)			CNV genotyped (post-QC)		
	Ancestry	**Cases**	**Controls**	**Total**	**Cases**	**Controls**	**Total**
Shanghai cohort	Han Chinese	735	750	1,485	722	750	1,472
Beijing cohort	Han Chinese	1,194	902	2,096	1,185	882	2,067
Combined cohorts	Han Chinese	1,929	1,652	3,581	1,907	1,632	3,539

Supplementary Table 3. Linkage disequilibrium between loci (Beijing cohort)

	rs10801555	**rs10754199**	**rs2019724**	**rs6428357**	**rs6677604**	**rs379489**	**rs2284664**	**rs1329428**	**rs1065489**	**rs11582939**	***CFHR3*Δ**	***CFHR1*Δ**
rs10801555		1.000	0.990	0.990	0.005	0.983	0.042	0.057	0.080	0.080	0.005	0.005
rs10754199	1.000		0.990	0.990	0.005	0.982	0.042	0.056	0.080	0.080	0.005	0.005
rs2019724	1.000	1.000		1.000	0.005	0.993	0.042	0.057	0.081	0.081	0.005	0.005
rs6428357	1.000	1.000	1.000		0.005	0.993	0.042	0.057	0.081	0.081	0.005	0.005
rs6677604	1.000	1.000	1.000	1.000		0.005	0.029	0.079	0.058	0.057	0.949	0.757
rs379489	0.993	0.993	1.000	1.000	1.000		0.044	0.059	0.081	0.081	0.005	0.005
rs2284664	0.981	0.981	0.982	0.982	0.968	1.000		0.744	0.538	0.538	0.025	0.026
rs1329428	0.986	0.986	0.987	0.987	1.000	1.000	0.999		0.725	0.724	0.078	0.055
rs1065489	0.988	0.988	0.988	0.988	1.000	0.988	0.995	0.998		1.000	0.058	0.037
rs11582939	0.988	0.988	0.988	0.988	1.000	0.988	0.995	0.998	1.000		0.058	0.037
***CFHR3*Δ**	1.000	1.000	1.000	1.000	0.981	1.000	0.906	0.988	1.000	1.000		0.058
***CFHR1*Δ**	1.000	1.000	1.000	1.000	0.923	1.000	0.864	0.789	0.753	0.752	1.000	

Right upper: R-square, left bottom: D’

Supplementary Table 4A. Haplotypes analysis in the Beijing cohort

Haplotype	Markers												Freq. Cases	Freq. Controls	Individual OR (95% CI)	Grouped OR (95% CI)
	rs10801555	rs10754199	rs2019724	rs6428357	rs6677604	rs379489	rs2284664	rs1329428	rs1065489	rs11582939	*CFHR3*Δ	*CFHR1*Δ				
H1: %	A	A	A	A	G	T	G	G	G	C	I	I	0.074	0.074	-reference-	-reference-
H2: #	G	G	G	G	A	C	G	A	G	C	D	D	0.036	0.068	0.54 (0.38, 0.77)**	0.52 (0.36, 0.74)**
H3:	G	G	G	G	G	C	A	A	G	C	D	D	0	0.003	0.14 (0.02, 1.25)	|
H4:	G	G	G	G	G	C	G	G	T	T	I	D	0.005	0.006	0.88 (0.34, 2.32)	0.92 (0.43, 1.96)
H5:	G	G	G	G	G	C	A	A	G	C	I	D	0.002	0.002	0.99 (0.14, 6.88)	|
H6:	G	G	G	G	A	C	G	A	G	C	D	I	0.003	0.003	0.82 (0.26, 2.63)	0.79 (0.25, 2.53)
H7: &	G	G	G	G	G	C	G	G	T	T	I	I	0.522	0.467	1.12 (0.88, 1.42)	1.03 (0.82, 1.30)
H8:	G	G	G	G	G	C	A	A	G	C	I	I	0.339	0.354	0.96 (0.75, 1.23)	|
H9:	G	G	G	G	G	C	G	A	G	C	I	I	0.014	0.018	0.76 (0.44, 1.30)	|
H10:	G	G	G	G	G	C	G	G	G	C	I	I	0.004	0.003	1.19 (0.42, 3.38)	|
Global Haplotype Test:															**P-value: 1.8*10-4**	**P-value: 8.1*10-5**

%: risk haplotype of AMD; #: protective haplotype of AMD and risk haplotype of aHUS; &: protective haplotype of N.meningitidis
| implied this haplotype grouped with the one above it, a: I: wild type; D: deletion

Supplementary Table 4B. Haplotypes analysis in the Beijing cohort using the more common H8 haplotype for reference.

Haplotype	Markers												Freq. Cases	Freq. Controls	Individual OR (95% CI)	Grouped OR (95% CI)
	rs10801555	rs10754199	rs2019724	rs6428357	rs6677604	rs379489	rs2284664	rs1329428	rs1065489	rs11582939	*CFHR3*Δ	*CFHR1*Δ				
H8:	G	G	G	G	G	C	A	A	G	C	I	I	0.339	0.354	-reference-	-reference-
H2: [#]	G	G	G	G	A	C	G	A	G	C	D	D	0.036	0.068	0.56 (0.42, 0.75)**	0.54 (0.41, 0.73)**
H3:	G	G	G	G	G	C	A	A	G	C	D	D	0	0.003	0.15 (0.02, 1.28)	|
H4:	G	G	G	G	G	C	G	G	T	T	I	D	0.005	0.006	0.92 (0.36, 2.35)	0.95 (0.46, 1.97)
H5:	G	G	G	G	G	C	A	A	G	C	I	D	0.002	0.002	1.03 (0.15, 7.07)	|
H6:	G	G	G	G	A	C	G	A	G	C	D	I	0.003	0.003	0.85 (0.27, 2.68)	0.86 (0.27, 2.72)
H7: [&]	G	G	G	G	G	C	G	G	T	T	I	I	0.522	0.467	1.16 (1.01, 1.33)	1.13 (0.99, 1.29)
H9:	G	G	G	G	G	C	G	A	G	C	I	I	0.014	0.018	0.79 (0.47, 1.31)	|
H10:	G	G	G	G	G	C	G	G	G	C	I	I	0.004	0.003	1.23 (0.45, 3.42)	|
H1: [%]	A	A	A	A	G	T	G	G	G	C	I	I	0.074	0.074	1.02(0.79,1.3)	|
Global Haplotype Test:															**P-value: 1.9*10-4**	**P-value: 1.8*10-5**

Supplementary Table 5A Allelic associations for rs6677604 and different copy number variants within *CFHR3* and *CFHR1* in the cohorts combined by meta-analysis.

	Cohorts Combined N=3,539 1,907 cases/1,632 controls				
	MAF (cases /controls)	OR	P-value	Q	I
rs6677604 (A)	0.044/0.071	0.61	2.5 x 10-6	0.22	33.3
CFHR3-CFHR1					
Del-Del	0.040/0.070	0.57	1.3 x 10-7	0.25	25.2
Wt-Del	0.0094/0.0098	0.99	0.98(NS)	0.67	0
Del-Wt	0.0039/0.0037	1.11	0.78(NS)	0.34	0
Wt-Dup	0.0037/0.0040	0.92	0.84(NS)	0.36	0

Supplementary Table 5B Conditional analysis rs6677604 and *CFHR3,1*Δ in the cohorts combined by meta-analysis.

		Cohorts Combined N=3,539 1,907 cases/1,632 controls			
Tested Variant	**Conditioning Variant**	OR	P-value	Q	I
rs6677604	none	0.61	2.5 x 10-6	0.22	33.3
rs6677604	Δ*CFHR3/CFHR1*	1.29	0.41	0.83	0
Δ*CFHR3/CFHR1*	none	0.57	1.3 x 10-7	0.25	25.2
Δ*CFHR3/CFHR1*	rs6677604	0.45	0.01	0.84	0

Supplementary Table 6. Pathology Oxford Scores by rs6677604.

	rs6677604			
Oxford Classification	**GG, N=531**	**AG /AA, N=84**	**OR (95%CI)***	**P-value***
M1 (%)	228 (42.9)	24 (28.6)	0.73 (0.43,1.23)	0.25
E1 (%)	267 (50.3)	42 (50.0)	1.33 (0.82,2.16)	0.25
S1 (%)	381 (71.8)	52 (61.9)	0.65 (0.40,1.07)	8.4×10^{-2}
T1 and T2 (%)	169 (31.8)	21 (25.0)	0.55 (0.31,0.93)	3.0×10^{-2}

M: Mesangial hypercellularity; E: Endocapillary hypercellularity; S: Segmental glomerulosclerosis; T: Tubular atrophy/interstitial fibrosis
* Effect sizes and P-values were adjusted by the cohort membership

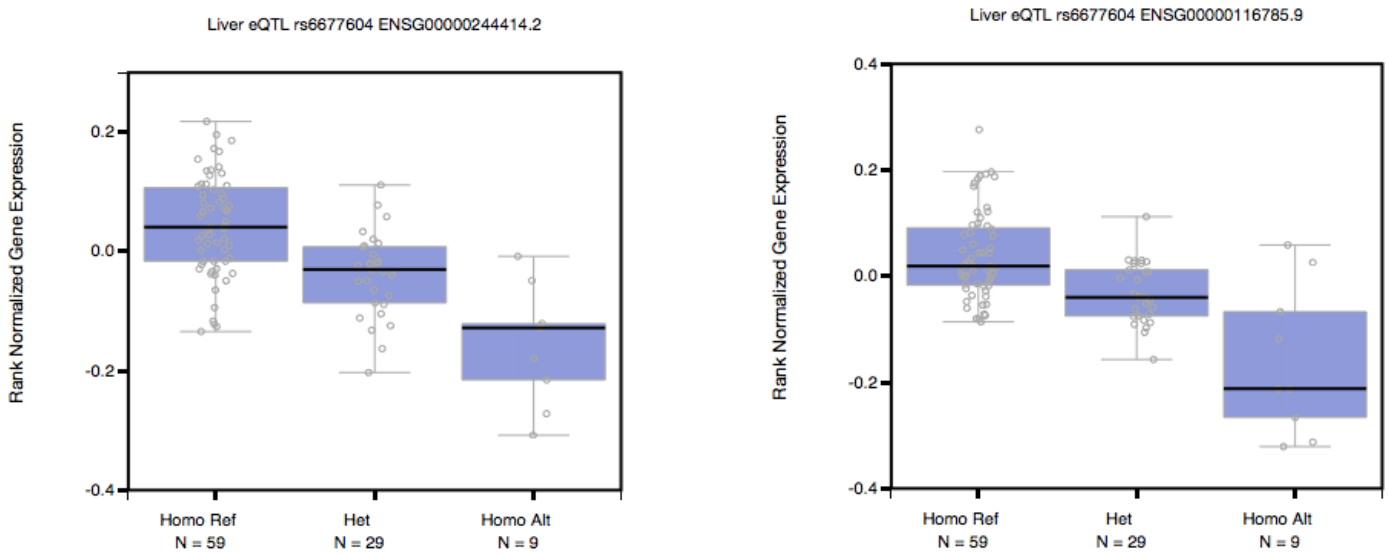
Supplementary Table 7. Association by Δ*CFHR3,CFHR1* with clinical parameters in the combined cohort

	Wt/Wt (N=1,767)	Wt/Del and Del/Del (N=149)	Effect Size* OR or Beta #	P-value*
Gender [Male %]	958 (54.2)	73 (49.0)	0.81 (0.58, 1.14)	0.23 (NS)
Age at biopsy (±s.d.), [years]	33.8±11.7	34.7±10.8	0.71 (-1.21, 2.63)	0.47(NS)
LN(eGFR) mean (±s.d.)	4.3±0.7	4.3±0.7	0.03 (-0.08, 0.14) #	0.64 (NS)
SBP mean (±s.d.), [mm Hg]	126.0±18.8	125.4±20.5	-0.89 (-4.04, 2.25) #	0.58 (NS)
DBP mean (±s.d.), [mm Hg]	80.3±13.2	80.2±13.7	-0.35 (-2.54, 1.84) #	0.75 (NS)
Gross hematuria (%)	480 (27.4)	31 (20.9)	0.73 (0.47, 1.09)	0.14 (NS)
Hyperuricemia (%)	518 (30.7)	39 (27.9)	1.21 (0.82, 1.80)	0.35 (NS)
Urine protein groups			-0.02 (-0.15, 0.11) #	0.79 (NS)
Mild (<1g/24h) (%)	711 (41.1)	65 (43.9)		
Moderate (1~3g/24h) (%)	654 (37.8)	51 (34.5)		
Severe (>=3g/24h) (%)	367 (21.2)	32 (21.6)		

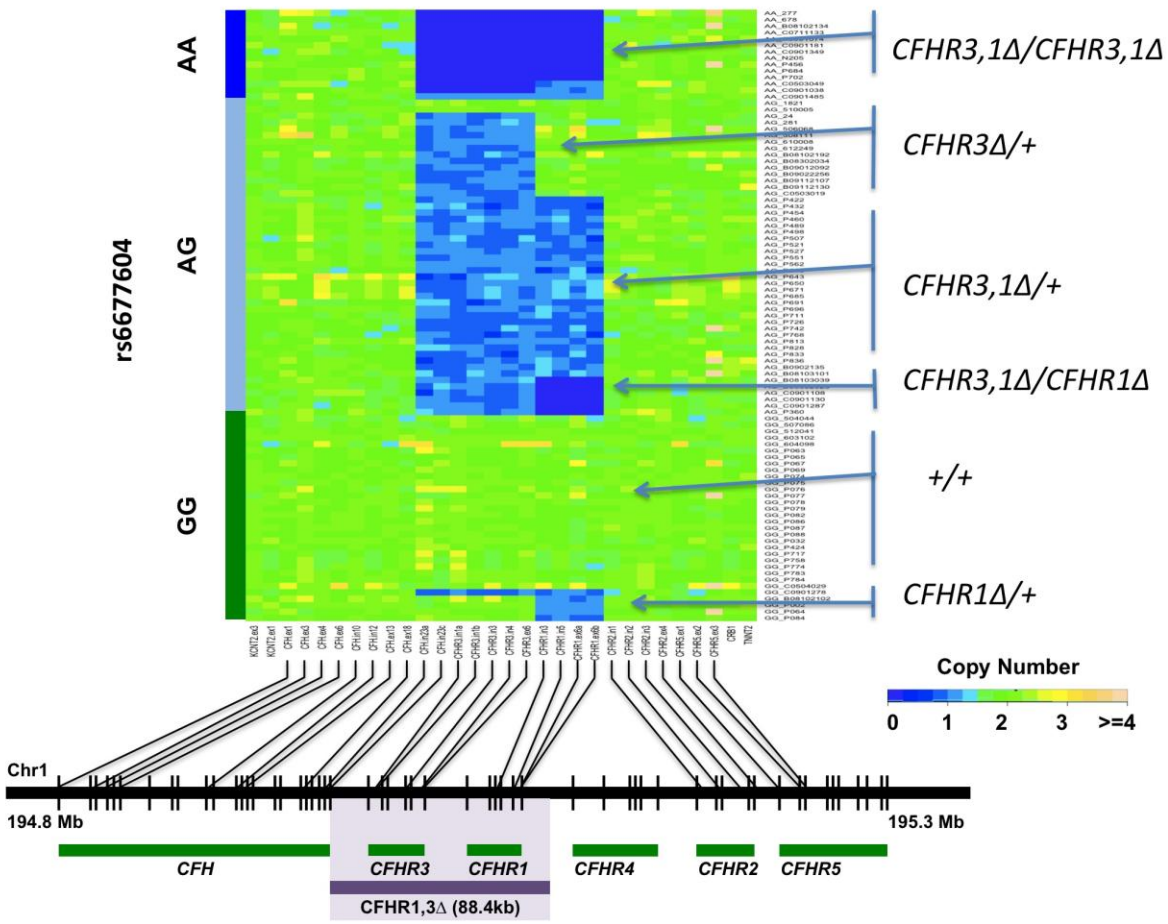
*** Effect size and P-value was adjusted by the cohort membership**

Supplementary Table 8. Samples that failed quality control in MLPA analysis

	rs6677604			
	AA	AG	GG	Total
IgAN patients	0	4	18	22
Healthy controls	0	4	16	20
Total	0	8	34	42



Supplementary Figure 1. Liver eQTL box plots by rs6677604 genotype for CFHR1 (Left) and CFHR3 (right). Genotype and number of samples are shown on X-axis. The Y-axis shows the Normalized values for CFHR1 and CFHR3 expression. Data from GTEx (reference 8)



Supplementary Figure 2. MLPA analysis of the CFH gene cluster showing examples of CNV genotypes and association with rs6677604 genotype. Each row represents an individual sample. The samples are grouped by rs6677604 genotype, indicated on Y-axis. The X-axis show the distribution of the MLPA probes across the *CFH* gene cluster, with corresponding genes below. The heatmap shows the different copy number variants (CNVs) detected across the region. Homozygous deletions are in deep blue, heterozygous deletions are in light blue, copy neutral regions are in green. The CNV genotypes are indicated on the right (+ indicates copy neutral alleles)