

Supplementary Table 1. The SNPs information used in PRS.

CHR	BP	Marker Name	A1	A2	Effect	StdErr	<i>P</i> value
6	32561656	rs9270599	A	G	0.4356	0.0384	3.936E-28
6	32632213	rs71542462	A	G	0.3758	0.0412	9.334E-19
8	6877468	rs11137085	C	G	0.2849	0.0327	3.002E-17
6	32640693	rs1694127	A	G	-0.4309	0.0524	1.559E-15
6	32577110	rs34328493	A	T	-0.3612	0.0462	3.471E-14
22	30423460	rs12537	T	C	-0.3012	0.0412	1.366E-12
6	33076268	rs742870	T	C	0.2332	0.0334	1.298E-11
6	31346822	rs9266629	T	C	-0.2424	0.0371	2.386E-10
6	29941769	rs437941	A	G	-0.2049	0.0314	2.513E-10
6	32582612	rs3104414	A	G	0.2315	0.036	4.542E-10
17	7459299	rs11078696	T	G	-0.2256	0.0351	4.633E-10
6	32455898	rs564813635	A	G	0.4119	0.0648	7.167E-10
6	32498932	rs546033671	T	G	-0.3945	0.0626	9.996E-10
6	32352616	rs9268465	T	C	-0.1992	0.0322	2.005E-09
8	6820255	rs75098331	T	C	0.2881	0.0483	7.353E-09
6	32594816	rs147599819	G	GGAT	0.2621	0.0446	1.218E-08
16	31377390	rs13332545	T	C	0.2194	0.0374	1.292E-08
6	32645076	rs55673904	T	C	0.223	0.0384	1.803E-08
22	30947033	rs116976860	A	G	-0.4264	0.0736	1.948E-08
6	32594191	rs150777477	T	G	-0.7114	0.1251	3.528E-08
4	40301264	rs11736377	T	C	-0.1844	0.0326	4.165E-08
6	32552664	rs551081202	T	C	-1.1177	0.198	4.436E-08
2	219188838	rs1473901	T	C	0.1441	0.0328	2.052E-05
6	155096462	rs10872710	T	C	0.2256	0.0527	3.323E-05
10	81065201	rs1250558	A	G	-0.1443	0.0325	1.674E-05
11	65559266	rs10791824	A	G	0.1296	0.0314	6.298E-05
22	21982054	rs1811069	T	G	-0.1281	0.033	0.0001677
14	103337253	rs8004192	T	C	-0.1347	0.0314	3.199E-05
16	72079657	rs77303550	T	C	-0.1698	0.0387	2.104E-05
21	29061536	rs80271593	A	C	0.4567	0.0995	8.596E-06

Notes: PRS: polygenic risk score; P value was adjusted by the intercept of LD score regression. The SNPs are from the meta-analysis and the integrative analysis.

Supplementary Table 2. Two missense variants at the significant loci associated with IgAN by GWAS meta-analysis.

Locus	Missense variant	Position	Ref/Alt	Amino Acid	PolyPhen	SIFT	Dataset 1			Dataset 2			Dataset 3			Meta	
							AF	OR (95% CI)	<i>P</i> value	AF	OR (95% CI)	<i>P</i> value	AF	OR (95% CI)	<i>P</i> value	OR (95% CI)	<i>P</i> value
<i>ITGAX</i>	rs2230429	16:31374535	C/G	Pro517Arg	0.997	0.003	0.25	1.21 (1.04~1.41)	1.27E-02	0.33	1.21 (1.09~1.33)	1.54E-04	0.33	1.31 (1.14~1.5)	1.15E-04	1.23 (1.15~1.33)	1.33E-08
<i>TNFSF13</i>	rs11552708	17:7462555	G/A	Gly67Arg	0.001	1	0.39	0.86 (0.76~0.98)	2.33E-02	0.32	0.83 (0.76~0.92)	1.36E-04	0.29	0.83 (0.72~0.96)	1.08E-02	0.84 (0.79~0.9)	7.66E-07

Notes: Ref: reference allele. Alt: alternative allele. AF: frequency of the reference allele. Odds ratio (OR) and 95% confidence interval (CI) of the alternative allele. Meta-analysis was based on inverse-variance weighted fixed-effect model. The *P* values of meta-analysis were adjusted by the intercept of LD score regression.

Supplementary Table 3. Associations of 60 established variants in our study.

SNP	Study (PMID)	Author, Year, Journal	Effect_allele	beta	P	Effect	P value	gcZ	gcP	Consequence	CHR	Position	Gene
rs2240335	32912934	Ming Li et al, 2020, J Am Soc Nephrol	A	0.10436	5.10E-09	0.0882	0.004716	2.741	0.006133	exonic	1	17674537	PADI4
rs17019602	25305756	Kirylyuk et al, 2014, Nat Genet	G	0.157004	6.80E-09	0.1003	0.009784	-2.506	0.01221	intronic	1	108188858	VAV3
rs849815	37337107	Ali G Gharavi et al, 2023, Nat Genet	A	0.131028	3.90E-09	0.0895	0.01483	2.364	0.01807	intergenic	1	157542162	FCRL5(dist=19857),FCRL4(dist=1376)
rs6427389	32912934	Ming Li et al, 2020, J Am Soc Nephrol	C	0.122218	8.18E-09	0.1783	3.15E-06	-4.525	6.04E-06	intergenic	1	157632011	FCRL4(dist=64136),FCRL3(dist=14260)
rs4916312	37337107	Ali G Gharavi et al, 2023, Nat Genet	A	0.131028	5.00E-08	0.0611	0.2412	1.135	0.2565	intergenic	1	173146357	TNFSF18(dist=126254),TNFSF4(dist=6513)
rs12029571	37337107	Ali G Gharavi et al, 2023, Nat Genet	A	0.113329	2.50E-06	0.0932	0.007707	2.582	0.009836	intergenic	1	196603302	KCNT2(dist=25732),CFH(dist=17706)
rs3766404	21399633	Kirylyuk et al, 2011, Nat Genet	C	-0.261365	4.24E-05	-0.1368	0.02206	2.221	0.02632	intronic	1	196651832	CFH
rs6677604	37337107	Ali G Gharavi et al, 2023, Nat Genet	G	0.19062	1.50E-17	0.254	0.0002781	-3.523	0.000427	intronic	1	196686918	CFH
rs842638	37337107	Ali G Gharavi et al, 2023, Nat Genet	T	0.157004	9.60E-10	0.1081	0.02991	2.104	0.03534	ncRNA_intronic	2	61092678	LINC01185
rs3769684	37337107	Ali G Gharavi et al, 2023, Nat Genet	T	0.173953	5.10E-11	0.0758	0.0157	2.34	0.01927	intronic	2	204584759	CD28
rs7634389	26028593	Ming Li et al, 2015, Nat Commun	C	0.122218	7.27E-10	0.1173	0.0002019	-3.61	0.0003061	intronic	3	186738421	ST6GAL1
rs6828610	37337107	Ali G Gharavi et al, 2023, Nat Genet	G	0.131028	3.50E-08	0.1174	0.0005483	-3.347	0.0008155	intergenic	4	74725320	PF4V1(dist=5120),CXCL1(dist=9790)
rs12201499	37337107	Ali G Gharavi et al, 2023, Nat Genet	C	0.165514	3.10E-11	0.1779	2.86E-06	-4.539	5.66E-06	intergenic	6	249571	LOC285766(dist=44087),DUSP22(dist=42486)
rs6942325	32912934	Ming Li et al, 2020, J Am Soc Nephrol	G	0.157004	1.62E-11	0.1817	1.81E-06	-4.623	3.78E-06	intergenic	6	249714	LOC285766(dist=44230),DUSP22(dist=42343)
rs12530084	37337107	Ali G Gharavi et al, 2023, Nat Genet	C	0.122218	1.30E-09	0.0553	0.07725	-1.713	0.08675	intronic	6	7214676	RREB1
rs2523946	22197929	Xue-Qing Yu et al, 2011, Nat Genet	C	0.19062	1.74E-11	0.2027	9.96E-11	-6.278	3.42E-10	upstream	6	29941943	HCG9(dist=949)
rs9268557	37337107	Ali G Gharavi et al, 2023, Nat Genet	C	0.215111	4.50E-47	0.1856	3.19E-09	-5.749	9.00E-09	intergenic	6	32389305	TSBP1-AS1(dist=13799),HLA-DRA(dist=18359)
rs7763262	25305756	Kirylyuk et al, 2014, Nat Genet	C	0.34359	1.80E-38	0.2663	2.86E-13	-7.073	1.52E-12	intergenic	6	32424882	HLA-DRA(dist=12059),HLA-DRB5(dist=60248)
rs660895	22197929	Xue-Qing Yu et al, 2011, Nat Genet	G	0.29267	4.13E-20	0.2741	4.37E-15	-7.614	2.66E-14	intergenic	6	32577380	HLA-DRB1(dist=19767),HLA-DQA1(dist=27803)
rs9272105	37337107	Ali G Gharavi et al, 2023, Nat Genet	A	0.223144	1.20E-28	0.2055	1.13E-08	5.534	3.13E-08	intergenic	6	32599999	HLA-DRB1(dist=42386),HLA-DQA1(dist=5184)
rs9275224	25305756	Kirylyuk et al, 2014, Nat Genet	G	0.307485	5.90E-30	0.2107	3.65E-09	-5.722	1.05E-08	intergenic	6	32659878	HLA-DQB1(dist=25444),HLA-DQA2(dist=49290)
rs9275355	37337107	Ali G Gharavi et al, 2023, Nat Genet	C	0.231112	1.70E-34	0.304	2.53E-18	-8.469	2.48E-17	intergenic	6	32667829	HLA-DQB1(dist=33395),HLA-DQA2(dist=41339)
rs2856717	25305756	Kirylyuk et al, 2014, Nat Genet	G	0.239017	1.10E-15	0.1488	0.0006742	-3.294	0.0009894	intergenic	6	32670308	HLA-DQB1(dist=35874),HLA-DQA2(dist=38860)
rs1794275	22197929	Xue-Qing Yu et al, 2011, Nat Genet	A	0.262364	3.43E-13	0.3475	1.01E-16	8.04	8.96E-16	intergenic	6	32671248	HLA-DQB1(dist=36814),HLA-DQA2(dist=37920)
rs9275596	37337107	Ali G Gharavi et al, 2023, Nat Genet	T	0.285179	3.20E-36	0.3712	7.11E-13	6.961	3.39E-12	intergenic	6	32681631	HLA-DQB1(dist=47197),HLA-DQA2(dist=27537)
rs9357155	21399633	Kirylyuk et al, 2011, Nat Genet	A	-0.34249	2.11E-12	-0.2244	1.88E-07	-5.048	4.48E-07	intronic	6	32809848	PSMB8
rs2071543	25305756	Kirylyuk et al, 2014, Nat Genet	G	0.139762	1.50E-04	0.2156	2.48E-07	-5	5.72E-07	exonic	6	32811629	PSMB8
rs3128927	37337107	Ali G Gharavi et al, 2023, Nat Genet	C	0.198851	1.50E-25	0.124	0.001358	-3.106	0.001895	intergenic	6	33074288	HLA-DPB1(dist=16815),HLA-DPB2(dist=6005)
rs1883414	25305756	Kirylyuk et al, 2014, Nat Genet	G	0.198851	1.50E-11	0.1378	0.0005496	-3.348	0.0008135	ncRNA_intronic	6	33086448	HLA-DPB2
rs2282859	37337107	Ali G Gharavi et al, 2023, Nat Genet	C	0.182322	3.90E-08	0.0607	0.1452	-1.411	0.1582	intronic	6	167445139	FGFR10P
rs3129269	21399633	Kirylyuk et al, 2011, Nat Genet	T	-0.235722	8.54E-09	-0.1426	0.0001286	-3.716	0.0002022	downstream	6	33097614	HLA-DPB2(dist=724)
rs2738048	25305756	Kirylyuk et al, 2014, Nat Genet	T	0.0953102	1.60E-04	0.2584	3.95E-14	7.325	2.39E-13	intergenic	8	6822785	DEFA9P(dist=5102),DEFA10P(dist=2878)
rs9314614	26028593	Ming Li et al, 2015, Nat Commun	C	0.131028	9.48E-10	0.1367	3.24E-05	4.028	5.62E-05	ncRNA_intronic	8	6697731	GS1-24F4.2
rs2075836	37337107	Ali G Gharavi et al, 2023, Nat Genet	T	0.19062	5.80E-11	0.252	2.38E-12	6.786	1.15E-11	ncRNA_intronic	8	6808722	DEFA8P
rs2738058	26028593	Ming Li et al, 2015, Nat Commun	T	0.239017	2.31E-27	0.279	2.68E-16	7.932	2.16E-15	intergenic	8	6821617	DEFA9P(dist=3934),DEFA10P(dist=4046)
rs12716641	26028593	Ming Li et al, 2015, Nat Commun	T	0.207014	1.13E-18	0.2068	2.91E-08	5.375	7.66E-08	intergenic	8	6898998	DEFA11P(dist=11987),DEFA5(dist=13828)
rs10086568	25305756	Kirylyuk et al, 2014, Nat Genet	A	0.14842	1.00E-09	0.1735	4.93E-07	4.875	1.09E-06	intergenic	8	6900336	DEFA11P(dist=13325),DEFA5(dist=12490)
rs75413466	37337107	Ali G Gharavi et al, 2023, Nat Genet	A	0.336472	1.40E-10	0.1359	0.05308	1.874	0.06092	intronic	8	56852496	LYN
rs2033562	26028593	Ming Li et al, 2015, Nat Commun	C	0.122218	1.41E-09	0.1188	0.0001275	3.715	0.000203	intergenic	8	103547739	UBR5(dist=122811),ODF1(dist=16078)
rs34354351	37337107	Ali G Gharavi et al, 2023, Nat Genet	T	0.139762	3.50E-08	0.0395	0.2492	1.116	0.2642	intergenic	8	124765474	ANXA13(dist=15841),FAM91A1(dist=15205)
rs13300483	37337107	Ali G Gharavi et al, 2023, Nat Genet	T	0.122218	1.30E-08	0.0517	0.1751	1.312	0.1895	intergenic	9	117643362	TNFSF15(dist=75043),TNFSF8(dist=12261)
rs4077515	37337107	Ali G Gharavi et al, 2023, Nat Genet	T	0.131028	2.60E-11	0.0688	0.03956	1.997	0.04583	exonic	9	139266496	CARD9
rs57917667	37337107	Ali G Gharavi et al, 2023, Nat Genet	G	0.198851	1.10E-08	0.061	0.1218	-1.501	0.1334	intronic	10	65363048	REEP3
rs1108618	37337107	Ali G Gharavi et al, 2023, Nat Genet	A	0.131028	1.90E-10	0.1061	0.001124	3.155	0.001604	intronic	10	81043743	ZMIZ1
rs2074038	26028593	Ming Li et al, 2015, Nat Commun	T	0.131028	3.93E-09	0.1157	0.0005915	3.328	0.0008735	5'UTR	11	44087989	ACCS(NM_032592:c.-11890>0)
rs10896045	37337107	Ali G Gharavi et al, 2023, Nat Genet	A	0.165514	4.70E-13	0.1228	8.67E-05	3.804	0.0001427	intronic	11	65555524	OVOL1
rs7121743	37337107	Ali G Gharavi et al, 2023, Nat Genet	C	0.122218	3.40E-08	0.065	0.03639	-2.026	0.04274	intergenic	11	128487069	ETS1(dist=29616),LOC101929538(dist=64066)
rs11150612	37337107	Ali G Gharavi et al, 2023, Nat Genet	A	0.14842	8.40E-14	0.1938	1.39E-08	5.51	3.59E-08	intergenic	16	31357760	ITGAM(dist=13562),ITGAX(dist=8737)
rs7190997	26028593	Ming Li et al, 2015, Nat Commun	C	0.198851	2.26E-19	0.2017	1.83E-08	-5.462	4.71E-08	intronic	16	31368178	ITGAX
rs1879210	37337107	Ali G Gharavi et al, 2023, Nat Genet	T	0.131028	9.90E-09	0.042	0.393	0.8276	0.4079	intergenic	16	86017715	IRF8(dist=61500),LINC01082(dist=212072)
rs3803800	37337107	Ali G Gharavi et al, 2023, Nat Genet	A	0.139762	1.20E-10	0.192	2.57E-09	5.781	7.44E-09	exonic	17	7462969	TNFSF12-TNFSF13,TNFSF13
rs4227	22197929	Xue-Qing Yu et al, 2011, Nat Genet	G	0.207014	4.31E-10	0.1609	9.10E-06	-4.297	1.73E-05	3'UTR	17	7491177	MPDU1(NM_001330073:c.*4150>0,NM_004870:c.*3080>0)
rs57382045	37337107	Ali G Gharavi et al, 2023, Nat Genet	A	0.14842	3.40E-09	0.1131	5.00E-04	3.374	0.0007416	intronic	17	16851450	TNFRSF13B
rs1865097	37337107	Ali G Gharavi et al, 2023, Nat Genet	A	0.113329	7.70E-09	0.0985	0.01056	2.48	0.01313	intronic	19	55397217	FCAR
rs12537	22197929	Xue-Qing Yu et al, 2011, Nat Genet	T	-0.248461	1.17E-11	-0.3012	2.68E-13	-7.087	1.37E-12	ncRNA_intronic	22	30423460	HORMAD2-AS1
rs2412971	25305756	Kirylyuk et al, 2014, Nat Genet	G	0.182322	4.80E-12	0.2458	9.08E-13	-6.927	4.29E-12	intronic	22	30494371	HORMAD2
rs4823074	37337107	Ali G Gharavi et al, 2023, Nat Genet	G	0.14842	7.80E-15	0.2498	5.83E-13	-6.979	2.97E-12	intronic	22	30512478	HORMAD2
rs2412973	21399633	Kirylyuk et al, 2011, Nat Genet	A	-0.223144	4.46E-09	-0.2423	1.46E-12	-6.868	6.49E-12	intronic	22	30529631	HORMAD2
rs751081288	37337107	Ali G Gharavi et al, 2023, Nat Genet	A	0.157004	1.90E-08	-	-	-	-	-	-	-	-
rs11574637	25305756	Kirylyuk et al, 2014, Nat Genet	T	0.277632	8.10E-13	-	-	-	-	-	-	-	-

Notes: gcZ, genomic control Z. gcZ was adjusted by the intercept of LDSC; gcP, genomic control P. gcP was calculated by adjusting gcZ values.

Supplementary Table 4. Clinical characteristics of the IgAN patients.	
Sample	Clinical characteristics
Age, median (IQR)	33 (26, 40)
Male (n, %)	1018 (45.2%)
Hypertension (n, %)	693 (31.6%)
Repeated GrossHematuria (n, %)	234 (10.4%)
IgA(g/L), median (IQR)	2.85 (2.24, 3.52)
C3(g/L), median (IQR)	0.97 (0.85, 1.11)
Serum creatinine (μmol/l), median (IQR)	86.00 (65.00, 128.00)
eGFR, median (IQR)	82.27 (51.10, 107.89)
Proteinuria	
≤ 1 g/24h	1186 (58.6%)
1~3.5 g/24h	634 (31.3%)
≥ 3.5 g/24h	205 (10.1%)
CKD stage(no.)	
CKD stage 1 (n, %)	921 (42.7%)
CKD stage 2 (n, %)	583 (27.0%)
CKD stage 3 (n, %)	407 (18.9%)
CKD stage 4 (n, %)	175 (8.1%)
CKD stage 5 (n, %)	71 (3.3%)
Mesangial hypercellularity (M1) (n, %)	1088 (62.4%)
Endocapillary hypercellularity (E1) (n, %)	285 (19.0%)
Segmental glomerulosclerosis (S1) (n, %)	801 (46.8%)
Tubular atrophy/Interstitial fibrosis	
T0 (n, %)	1163 (67.7%)
T1 (n, %)	433 (25.2%)
T2 (n, %)	123 (7.2%)
Crescent formation	
C0 (n, %)	568 (58.1%)
C1 (n, %)	356 (36.4%)
C2 (n, %)	54 (5.5%)

Supplementary Table 5. Genotype-phenotype association in IgAN cases.The IgAN susceptibility SNPs were tested for associations with clinical features of disease severity at the time of kidney biopsy. The association analysis was performed using the logistic regression for binary and ordinal variables and linear regression for quantitative traits under additive model with adjustment for age and gender. Suggestive associations at nominal $P < 0.05$ were highlighted in yellow.

SNP effect allele	Gene	Hypertension		Repeated Gross Hematuria		CKD stage		Mesangial hypercellularity		Endocapillary hypercellularity		Segmental glomerulosclerosis		Tubular atrophy/Interstitial fibrosis		Crescent		Proteinuria		IgA (g/L)		C3 (g/L)		SCr (umol/L)		eGFR	
		OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>	Beta (95% CI)	<i>P</i>	Beta (95% CI)	<i>P</i>	Beta (95% CI)	<i>P</i>	Beta (95% CI)	<i>P</i>	Beta (95% CI)	<i>P</i>
rs1473901_C	<i>PNKD</i>	0.973 (0.849~1.117)	0.703	0.915 (0.748~1.119)	0.388	1.014 (0.903~1.138)	0.812	1.063 (0.921~1.226)	0.402	1.064 (0.881~1.284)	0.514	0.92 (0.801~1.058)	0.246	1.028 (0.888~1.191)	0.71	0.87 (0.718~1.055)	0.155	1.061 (0.936~1.203)	0.358	-0.028 (-0.052~-0.004)	0.017	-0.014 (-0.032~0.004)	0.101	0.013 (-0.02~0.046)	0.467	-0.019 (-0.06~0.022)	0.367
rs11736377_C	<i>LOC101060498</i>	0.93 (0.812~1.064)	0.287	0.971 (0.799~1.182)	0.771	1.017 (0.91~1.137)	0.764	1.112 (0.965~1.28)	0.138	1.021 (0.848~1.23)	0.822	0.959 (0.836~1.1)	0.549	0.998 (0.865~1.152)	0.978	1.191 (0.997~1.424)	0.054	0.933 (0.825~1.056)	0.273	-0.008 (-0.032~0.016)	0.502	0.006 (-0.012~0.024)	0.46	-0.006 (-0.039~0.027)	0.7	0.013 (-0.028~0.054)	0.541
rs10872710_T	<i>SCAF8</i>	0.843 (0.674~1.054)	0.133	0.88 (0.632~1.225)	0.45	0.913 (0.759~1.098)	0.333	0.909 (0.726~1.139)	0.407	0.969 (0.715~1.314)	0.843	0.893 (0.717~1.112)	0.315	0.898 (0.709~1.136)	0.368	0.947 (0.712~1.261)	0.709	1.004 (0.824~1.224)	0.967	-0.025 (-0.062~0.012)	0.186	0.005 (-0.022~0.032)	0.728	-0.028 (-0.081~0.025)	0.315	0.044 (-0.023~0.111)	0.192
rs8004192_C	<i>TRAF3</i>	1.111 (0.972~1.269)	0.12	1.05 (0.865~1.275)	0.621	1.105 (0.99~1.233)	0.075	1.048 (0.914~1.202)	0.505	1.151 (0.96~1.382)	0.129	1.097 (0.959~1.256)	0.175	1.101 (0.956~1.268)	0.184	1.142 (0.956~1.365)	0.144	0.971 (0.86~1.097)	0.642	0.008 (-0.014~0.03)	0.456	-0.003 (-0.021~0.015)	0.719	0.012 (-0.021~0.045)	0.471	-0.015 (-0.054~0.024)	0.467
rs77303550_T	<i>TXNL4B</i>	1.013 (0.871~1.178)	0.869	1.053 (0.847~1.309)	0.64	0.949 (0.836~1.078)	0.427	0.922 (0.79~1.077)	0.305	0.979 (0.796~1.205)	0.842	1.084 (0.931~1.263)	0.301	1.028 (0.876~1.208)	0.734	0.888 (0.724~1.089)	0.252	0.864 (0.75~0.995)	0.043	-0.008 (-0.033~0.017)	0.508	0 (-0.02~0.02)	0.962	-0.002 (-0.039~0.035)	0.908	-0.001 (-0.046~0.044)	0.97
rs80271593_A	<i>LINC00113</i>	1.153 (0.799~1.663)	0.447	1.354 (0.825~2.223)	0.231	0.901 (0.661~1.228)	0.509	0.986 (0.662~1.468)	0.943	1.53 (0.956~2.448)	0.076	0.98 (0.668~1.439)	0.917	0.905 (0.601~1.363)	0.633	0.97 (0.588~1.603)	0.906	1.302 (0.933~1.817)	0.12	0.039 (-0.024~0.102)	0.219	0.036 (-0.011~0.083)	0.131	-0.037 (-0.129~0.055)	0.426	0.021 (-0.093~0.135)	0.713
rs1811069_T	<i>UBE2L3</i>	0.9 (0.786~1.031)	0.127	1.043 (0.857~1.269)	0.673	0.989 (0.885~1.106)	0.847	0.889 (0.773~1.021)	0.097	0.984 (0.819~1.183)	0.862	0.953 (0.831~1.093)	0.493	0.955 (0.826~1.104)	0.531	0.914 (0.762~1.097)	0.33	0.946 (0.837~1.071)	0.388	-0.001 (-0.023~0.021)	0.911	-0.005 (-0.023~0.013)	0.581	-0.013 (-0.046~0.02)	0.432	0.007 (-0.034~0.048)	0.754

Supplementary Table 6. Genotype-phenotype association between the PRS and disease severity in IgAN cases. The association analysis was performed using the linear regression for quantitative traits with adjustment for age and gender. Suggestive associations at nominal $P < 0.05$ were highlighted in yellow.

	Hypertension		Repeated Gross Hematuria		CKD stage		Mesangial hypercellularity		Endocapillary hypercellularity		Segmental glomerulosclerosis		Tubular atrophy/Interstitial fibrosis		Crescent		Proteinuria		IgA (g/L)		C3 (g/L)		SCr (umol/L)		eGFR	
	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>	Beta (95% CI)	<i>P</i>	Beta (95% CI)	<i>P</i>	Beta (95% CI)	<i>P</i>	Beta (95% CI)	<i>P</i>
The PRS	-0.028 (-0.030~-0.006)	0.181	0.002 (-0.010~-0.014)	0.727	0.039 (-0.004~-0.0081)	0.076	0.046 (0.024~-0.068)	5.20E-05	-0.014 (-0.032~-0.005)	0.157	0.024 (0.001~-0.047)	0.039	0.016 (-0.012-0.045)	0.255	-0.023 (-0.076~-0.030)	0.394	0.099 (0.022~-0.176)	0.012	0.020 (-0.026-0.065)	0.396	-0.014 (-0.026~-0.001)	0.029	1.470 (-3.855~-6.795)	0.588	-1.778 (-3.396~-0.161)	0.031

Supplementary Table 7. Associations between seven novel loci and the prognosis of IgAN. Cox proportional hazards model was adjusted for age at diagnosis, gender, hypertension, proteinuria, and eGFR.

SNP_effect allele	Gene	HR (95% CI)	<i>P</i>	Adjusted HR (95% CI)	Adjusted <i>P</i>
rs1473901_C	<i>PNKD</i>	1.046 (0.75~1.458)	0.793	1.192 (0.849~1.674)	0.311
rs11736377_C	<i>LOC101060498</i>	1.076 (0.766~1.51)	0.673	1.404 (0.98~2.011)	0.064
rs10872710_T	<i>SCAF8</i>	1.136 (0.667~1.934)	0.64	1.395 (0.834~2.332)	0.204
rs8004192_C	<i>TRAF3</i>	1.036 (0.754~1.425)	0.826	1.058 (0.758~1.475)	0.741
rs77303550_T	<i>TXNL4B</i>	1.085 (0.748~1.574)	0.667	0.947 (0.637~1.409)	0.790
rs80271593_A	<i>LINC00113</i>	1.308 (0.575~2.978)	0.522	0.921 (0.428~1.982)	0.833
rs1811069_T	<i>UBE2L3</i>	1.234 (0.876~1.738)	0.229	1.406 (0.997~1.984)	0.052

Supplementary Table 8. Association between the PRS and the prognosis of IgAN. Cox proportional hazards model was adjusted for age at diagnosis, gender, hypertension, proteinuria, and eGFR.

	HR (95% CI)	<i>P</i>	Adjusted HR (95% CI)	Adjusted <i>P</i>
The PRS	0.885 (0.732~1.069)	0.204	0.784 (0.649~0.945)	0.011

Supplementary Table 9. Significant eQTLs effects for lead SNPs in the novel loci based on GTEx (v8) data.

Lead SNP in the novel loci	Tissue	<i>P</i> value	Gene
rs1473901	Skin - Sun Exposed (Lower leg)	2.30E-66	<i>PNKD</i>
	Skin - Not Sun Exposed (Suprapubic)	6.10E-44	<i>PNKD</i>
	Thyroid	8.90E-31	<i>PNKD</i>
	Whole Blood	1.60E-25	<i>PNKD</i>
	Adrenal Gland	1.30E-20	<i>PNKD</i>
	Testis	4.60E-20	<i>PNKD</i>
	Pituitary	6.60E-16	<i>PNKD</i>
	Adipose - Visceral (Omentum)	7.00E-12	<i>PNKD</i>
	Spleen	2.30E-11	<i>PNKD</i>
	Heart - Atrial Appendage	2.40E-11	<i>PNKD</i>
	Adipose - Subcutaneous	1.10E-10	<i>PNKD</i>
	Lung	2.90E-08	<i>PNKD</i>
	Brain - Caudate (basal ganglia)	3.20E-08	<i>PNKD</i>
	Brain - Nucleus accumbens (basal ganglia)	5.10E-07	<i>PNKD</i>
	Liver	0.0000072	<i>PNKD</i>
	Brain - Putamen (basal ganglia)	0.000012	<i>PNKD</i>
	Artery - Aorta	0.000012	<i>PNKD</i>
Cells - Cultured fibroblasts	0.000077	<i>PNKD</i>	
rs1811069	Whole Blood	5.40E-24	<i>UBE2L3</i>
	Muscle - Skeletal	1.30E-13	<i>UBE2L3</i>
	Esophagus - Mucosa	2.50E-09	<i>UBE2L3</i>
	Esophagus - Muscularis	3.60E-09	<i>UBE2L3</i>
	Nerve - Tibial	5.30E-08	<i>UBE2L3</i>
	Testis	7.40E-08	<i>UBE2L3</i>
	Esophagus - Gastroesophageal Junction	6.90E-07	<i>UBE2L3</i>
	Skin - Sun Exposed (Lower leg)	0.0000015	<i>UBE2L3</i>
	Artery - Tibial	0.000046	<i>UBE2L3</i>
	Adipose - Subcutaneous	0.00011	<i>UBE2L3</i>
rs8004192	Esophagus - Mucosa	6.50E-08	<i>TRAF3</i>
	Brain - Hypothalamus	6.70E-08	<i>TRAF3</i>
	Brain - Cortex	2.70E-07	<i>TRAF3</i>
	Thyroid	0.0000038	<i>TRAF3</i>
	Brain - Spinal cord (cervical c-1)	0.0000092	<i>TRAF3</i>
rs77303550	Cells - Cultured fibroblasts	0.00039	<i>TXNL4B</i>

Supplementary Table 10. Functional annotation of seven significant loci by CADD, RegulomeDB and chromatin looping database.

SNP	CADD score	Regulome DB score	RegulomeDB rank	ChromLoops
rs11736377	2.279	0.000	6	Loop SNP result - ChromLoops (hzau.edu.cn)
rs1473901	15.030	0.762	2b	Loop SNP result - ChromLoops (hzau.edu.cn)
rs1811069	1.930	0.590	5	
rs10872710	0.154	0.590	5	
rs77303550	0.320	0.520	3a	
rs80271593	2.631	0.133	5	
rs8004192	0.125	0.609	4	

Supplementary Table 11. Functional annotation of the variants that are highly correlated ($r^2 > 0.7$) with the seven lead SNPs and nominally significant ($P < 0.05$) at each novel locus based on FUMA data.

rsID	chr	pos	non_ref_allele	effect_allele	MAF	gwasP	r ² SNP	IndSigSNP	Gene	nearest Gene	dist	func	CADD	RDB	posMapFilt	eqtMapFilt	ciMapFilt
rs21915108	2	21911518	G	A	0.4128	7.83E-05	0.75399	rs1473901	1	ARBC2	0	intronic	0.207	7	1	1	0
rs736730	2	21912025	C	T	0.4125	5.82E-05	0.735398	rs1473901	1	RP11-378A13.1	0	ncRNA_exonic	1.992	1d	1	1	0
rs736731	2	21912058	G	A	0.4125	0.000108	0.735398	rs1473901	1	RP11-378A13.1	0	ncRNA_exonic	0.251	NA	1	1	0
rs12999734	2	21912158	G	A	0.4125	0.000108	0.735398	rs1473901	1	RP11-378A13.1	0	ncRNA_exonic	0.818	5	1	1	0
rs10932766	2	21912209	G	A	0.4125	8.98E-05	0.735398	rs1473901	1	RP11-378A13.1	2	downstream	5.58	2b	1	1	0
rs3731859	2	21912422	G	A	0.4125	7.54E-05	0.735398	rs1473901	1	GPBAR1	0	5'UTR	0.039	4	1	1	0
rs3033334	2	21912491	T	A	0.4125	7.09E-05	0.735398	rs1473901	1	GPBAR1	0	intronic	3.676	5	1	1	0
rs11554825	2	21912589	C	T	0.4125	2.93E-05	0.735398	rs1473901	1	GPBAR1	0	5'UTR	3.726	4	1	1	0
rs13419763	2	21913459	C	T	0.4165	2.36E-05	0.728893	rs1473901	1	AAMP	0	5'UTR	5.706	4	1	1	0
rs10716631	2	21913817	G	T	0.4195	6.70E-05	0.720117	rs1473901	1	PNKD	0	intronic	2.998	6	1	1	0
rs4791	2	21913894	C	T	0.4185	5.83E-05	0.724287	rs1473901	1	PNKD-TMBIM1	0.00	3'UTR	16.66	6	1	1	0
rs4674280	2	21914158	G	C	0.4165	4.97E-05	0.716695	rs1473901	1	PNKD-TMBIM1	0.00	intronic	0.245	5	1	1	0
rs2168704	2	21914242	G	A	0.4165	6.69E-05	0.729818	rs1473901	1	PNKD-TMBIM1	0.00	intronic	3.129	7	1	1	0
rs13429408	2	21914260	C	A	0.4165	6.93E-05	0.729818	rs1473901	1	PNKD-TMBIM1	0.00	intronic	2.127	5	1	1	0
rs2292553	2	21914680	C	A	0.4165	6.13E-05	0.729818	rs1473901	1	PNKD-TMBIM1	0.00	intronic	13.62	5	1	1	0
rs2182826	2	21914873	C	A	0.4175	5.8E-05	0.727516	rs1473901	1	PNKD-TMBIM1	0.00	intronic	1.211	7	1	1	0
rs5582343	2	21914978	G	A	0.4145	5.75E-05	0.728821	rs1473901	1	PNKD-TMBIM1	0.00	intronic	0.013	7	1	1	0
rs5610829	2	21914970	G	A	0.4145	5.75E-05	0.728821	rs1473901	1	PNKD-TMBIM1	0.00	intronic	0.408	7	1	1	0
rs992157	2	21915478	G	A	0.4165	4.69E-05	0.729818	rs1473901	1	PNKD-TMBIM1	0.00	5'UTR	7.302	1f	1	1	0
rs56344368	2	21916074	C	T	0.4195	2.87E-05	0.773658	rs1473901	1	PNKD	0	intronic	4.029	7	1	1	0
rs13427681	2	21916753	G	C	0.4195	3.14E-05	0.773658	rs1473901	1	PNKD	0	intronic	3.604	7	1	1	0
rs1877712	2	21916843	G	A	0.4195	3.06E-05	0.773658	rs1473901	1	PNKD	0	intronic	11.98	NA	1	1	0
rs4672884	2	21918241	G	A	0.3887	2.69E-05	0.973251	rs1473901	1	PNKD	0	intronic	0.37	5	1	1	0
rs13424679	2	21918419	G	A	0.34	3.64E-05	0.802637	rs1473901	1	PNKD	0	intronic	2.898	7	1	1	0
rs2382825	2	21918427	C	T	0.34	3.64E-05	0.802637	rs1473901	1	PNKD	0	intronic	0.688	6	1	1	0
rs2382826	2	21918428	G	A	0.34	3.74E-05	0.802637	rs1473901	1	PNKD	0	intronic	0.112	7	1	1	0
rs2891075	2	21918430	G	A	0.34	3.74E-05	0.802637	rs1473901	1	PNKD	0	intronic	0.99	7	1	1	0
rs2828227	2	21918437	G	A	0.34	3.83E-05	0.802637	rs1473901	1	PNKD	0	intronic	0.012	7	1	1	0
rs2891076	2	21918438	C	T	0.34	3.74E-05	0.802637	rs1473901	1	PNKD	0	intronic	3.305	2b	1	1	0
rs2891077	2	21918443	C	T	0.338	5.02E-05	0.797232	rs1473901	1	PNKD	0	intronic	8.533	7	1	1	0
rs2891078	2	21918443	C	T	0.338	5.02E-05	0.797232	rs1473901	1	PNKD	0	intronic	7.824	7	1	1	0
rs13020391	2	21918446	C	T	0.337	4.16E-05	0.787572	rs1473901	1	PNKD	0	intronic	7.183	7	1	1	0
rs2382828	2	21918449	G	A	0.34	3.64E-05	0.802637	rs1473901	1	PNKD	0	intronic	6.62	7	1	1	0
rs2382829	2	21918461	G	A	0.341	3.64E-05	0.805372	rs1473901	1	PNKD	0	intronic	4.242	5	1	1	0
rs2891079	2	21918469	G	A	0.341	3.64E-05	0.805372	rs1473901	1	PNKD	0	intronic	5.972	5	1	1	0
rs4280446	2	21918472	C	T	0.341	3.64E-05	0.805372	rs1473901	1	PNKD	0	intronic	6.435	5	1	1	0
rs4525182	2	21918472	G	T	0.341	3.77E-05	0.805372	rs1473901	1	PNKD	0	intronic	3.788	5	1	1	0
rs4423579	2	21918503	G	T	0.341	3.64E-05	0.805372	rs1473901	1	PNKD	0	intronic	4.069	5	1	1	0
rs2015863	2	21918516	C	T	0.34	3.21E-05	0.795595	rs1473901	1	PNKD	0	intronic	0.805	NA	1	1	0
rs4672886	2	21918545	G	A	0.341	3.77E-05	0.805372	rs1473901	1	PNKD	0	intronic	4.984	1f	1	1	0
rs57851860	2	21918642	C	T	0.341	3.64E-05	0.805372	rs1473901	1	PNKD	0	intronic	3.551	6	1	1	0
rs62183964	2	21918692	G	A	0.341	3.64E-05	0.805372	rs1473901	1	PNKD	0	intronic	1.651	7	1	1	0
rs10203039	2	21918767	C	T	0.3907	3.42E-05	0.988513	rs1473901	1	PNKD	0	intronic	8.19	2b	1	1	0
rs10319189	2	21918783	C	A	0.34	4.98E-05	0.802637	rs1473901	1	PNKD	0	intronic	3.305	2b	1	1	0
rs2870123	2	21918798	G	A	0.341	4.98E-05	0.805372	rs1473901	1	PNKD	0	intronic	2.876	2b	1	1	0
rs1870124	2	21918770	C	T	0.341	3.00E-05	0.805372	rs1473901	1	PNKD	0	intronic	8.761	4	1	1	0
rs1870125	2	21918790	C	T	0.3917	2.47E-05	0.992383	rs1473901	1	PNKD	0	5'UTR	10.45	4	1	1	0
rs10194082	2	21918877	C	T	0.3907	2.25E-05	0.99617	rs1473901	1	PNKD	0	intronic	10.51	4	1	1	0
rs62183995	2	21918965	G	A	0.338	1.84E-05	0.803709	rs1473901	1	PNKD	0	intronic	0.203	7	1	1	0
rs3731861	2	21919125	C	T	0.3439	2.60E-05	0.779124	rs1473901	1	PNKD	0	intronic	8.982	5	1	1	0
rs10932774	2	21919156	G	A	0.3429	2.62E-05	0.783365	rs1473901	1	PNKD	0	intronic	8.904	1f	1	1	0
rs987877	2	21919275	G	A	0.3907	1.83E-05	0.965614	rs1473901	1	PNKD-AC01016.8	0.00	ncRNA_intronic	5.192	1f	1	1	0
rs6832151	4	40303633	G	T	0.2773	1.36E-07	0.971938	rs11736377	2	AC195454.1	14868	intergenic	2.962	1f	0	0	0
rs4078470	4	40305745	T	A	0.3121	0.001697	0.916289	rs11736377	2	AC195454.1	12756	intergenic	0.063	NA	0	0	0
rs4379091	4	40306373	G	T	0.2773	9.17E-08	0.968638	rs11736377	2	AC195454.1	12128	intergenic	0.586	NA	0	0	0
rs13136820	4	40307564	C	T	0.236	1.17E-07	0.753448	rs11736377	2	AC195454.1	10937	intergenic	3.997	4	0	0	0
rs7691190	4	40308368	C	T	0.2962	1.23E-07	0.861405	rs11736377	2	AC195454.1	10133	intergenic	1.567	4	0	0	0
rs5971823	6	155028910	C	T	0.499	0.0008859	0.779109	rs10827210	3	RP11-15G1.1	0	ncRNA_exonic	1.223	5	0	0	0
rs737367	6	15502910	G	A	0.462	0.002849	0.923644	rs10827210	3	RP11-15G1.1	0	ncRNA_exonic	0.463	5	0	0	0
rs9397740	6	15504250	G	A	0.4702	0.0007245	0.765603	rs10827210	3	SCAF8	11957	intergenic	0.463	5	0	0	0
rs292533	6	15504359	G	A	0.4712	0.0007299	0.768885	rs10827210	3	SCAF8	10863	intergenic	0.201	7	0	0	0
rs9371349	6	15504463	C	T	0.4702	0.0005299	0.764802	rs10827210	3	SCAF8	9825	intergenic	1.017	6	0	0	0
rs9397741	6	15504737	C	T	0.4801	0.001178	0.823625	rs10827210	3	SCAF8	7087	intergenic	0.284	7	1	0	0
rs6932758	6	15504919	C	T	0.492	0.0001482	0.725719	rs10827210	3	SCAF8	5265	intergenic	6.626	7	1	0	0
rs6932958	6	15504931	C	T	0.494	0.000146	0.712284	rs10827210	3	SCAF8	5140	intergenic	0.508	6	1	0	0
rs3828933	6	15505397	C	T	0.4841	0.0005132	0.70113	rs10827210	3	SCAF8	485	upstream	11.27	NA	1	0	0
rs452651	6	15505519	G	A	0.4791	0.00011	1	rs10827210	3	SCAF8	0	intronic	13.99	4	1	0	