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Supplemental Material

IgA Nephropathy Susceptibility Loci and Disease Progression

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Table S1 | Linkage Disequilibrium Analyses Between the Selected Single Nucleotide Polymorphisms.

	rs1883414	rs7763262	rs9275224	rs2856717	rs9275596	rs2738048	rs12716641	rs9314614	rs2071543	rs2412971	rs3803800	rs17019602	rs11150612	rs2033562	rs2074038	rs7634389
rs1883414		0.76	0.71	0.50	0.50	0.23	0.21	0.71	0.90	0.90	0.54	0.29	0.35	0.58	0.50	0.58
rs7763262	0.01		0.03	0.09	0.16	0.16	0.50	0.42	0.01	0.50	0.23	0.71	0.81	0.90	0.12	0.71
rs9275224	0.05	0.2		<0.001	0.02	0.23	0.46	0.26	0.09	0.62	1	0.76	0.95	0.76	0.11	0.67
rs2856717	0.02	0.03	**0.38***		<0.001	0.90	0.76	0.85	0.08	0.85	0.95	0.38	0.81	0.54	0.02	0.21
rs9275596	0.01	0.04	0.18	**0.53***		0.90	0.50	0.95	0.14	0.95	0.67	0.26	0.81	0.71	0.05	0.07
rs2738048	0	0.02	0	0	0		<0.001	0.04	0.42	0.42	0.76	0.12	0.62	0.16	0.71	0.54
rs12716641	0	0.01	0	0	0	**0.21***		0.01	0.62	0.62	1	0.11	0.42	0.08	0.76	0.11
rs9314614	0	0	0	0	0	0	0.01		0.46	0.90	0.90	0.76	0.76	0.23	0.95	0.50
rs2071543	0	0.01	0.01	0.05	0.07	0.01	0	0		0.38	0.90	0.67	0.85	0.76	0.11	0.29
rs2412971	0	0	0	0	0	0	0	0	0		0.90	0.85	0.35	0.76	0.67	0.67
rs3803800	0	0	0	0	0	0	0	0	0	0		0.76	0.58	0.76	0.58	0.76
rs17019602	0	0	0	0.01	0.01	0	0	0	0	0	0		0.26	0.81	0.38	0.46
rs11150612	0.01	0	0	0	0	0	0	0	0	0	0	0.26		1	0.38	0.54
rs2033562	0	0	0	0	0	0	0	0.01	0	0	0.01	0	0		1	0.46
rs2074038	0	0	0	0	0	0	0	0	0	0	0	0	0.01	0		0.62
rs7634389	0	0	0	0	0	0.01	0.01	0	0	0	0	0	0	0	0	

Linkage disequilibrium structure between SNPs in our study: r^2 (below the diagonal) and P value (above the diagonal).

*Significant by Bonferroni-adjusted P (P value <0.05/16).

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Table S2 | Haplotype analyses of the *HLA-DQ/DR* region rs7763262, rs9275224, rs2856717 and rs9275596.

Haplotype	Frequency			OR (95% CI)
	Total	Progressive group [a]	Non-progressive group [b]	
CGCT	0.65	0.65	0.66	ref
TATC	0.05	0.06	0.04	0.88 (0.30, 2.59)
CATC	0.05	0.06	0.05	0.62 (0.18, 2.12)
CGCC	0.04	0.06	0.03	2.98 (0.73, 12.20)
CATT	0.04	0.07	0.03	2.45 (0.89, 6.70)
TACT	0.07	0.05	0.08	0.70 (0.25, 1.91)
CACT	0.05	0.03	0.05	0.55 (0.16, 1.93)
TGCT	0.05	0.03	0.06	0.45 (0.11, 1.78)

Frequency of progressive group [a] was the haplotype frequency of progressive patients (progressed to combined outcome within 5 years).

Frequency of non-progressive group [b] was the haplotype frequency of non-progressive patients (combined-outcome free within 5 years).

The most common haplotype (CGCT) was used for reference.

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Table S3 | Comparison of Different Genetic Risk Scores Equations on Disease Prediction

Genetic Risk Score Equations	R Square	C-statistics (95%CI)	Model 1		Model 2		Model 3	
			HR (95%CI)	P	HR (95%CI)	P	HR (95%CI)	P
Genetic Risk Score[a]	3.10%	0.63 (0.55, 0.72)	1.65 (1.29, 2.11)	<0.001	1.29 (1.03, 1.62)	0.03	1.35 (1.03, 1.77)	0.03
Standardized Genetic Risk Score[b]	0.20%	0.45 (0.36, 0.54)	0.76 (0.46, 1.26)	0.28	0.93 (0.58, 1.50)	0.76	1.01 (0.59, 1.70)	0.99
Unweighted 9-SNP Genetic Risk Score[c]	0.30%	0.53 (0.44, 0.63)	0.95 (0.87, 1.03)	0.23	1.02 (0.94, 1.11)	0.57	0.99 (0.90, 1.10)	0.87

Genetic Risk Score[a]: unweighted 4-SNP genetic risk score equation derived from this study.

Standardized Genetic Risk Score[b]: weighted 15-SNP genetic risk score equation from Kiryluk K et al (*Kiryluk K* et al, Nat Genet. 2014)

Standardized Genetic Risk =

[0.16 × N(rs17019602:G) - 0.22 × N(rs7763262:T) - 0.29 × N(rs9275224:A) + 0.48 × N(rs2856717:T) - 0.42 × N(rs9275596:C) - 0.17 × N(rs2071543:A) - 0.19 × N(rs1883414:T) - 0.06 × N(rs2738048:C) + 0.1 × N(rs11150612:A) + 0.15 × N(rs3803800:A) + 0.17 × N(rs2412971:A) – Worldwide Mean] / (Worldwide SD)

N = number of reference alleles for each SNP (0, 1, or 2 per individual genotype).

Worldwide Mean = -0.002188 = mean risk score based on the HGDP data.

Worldwide SD = 0.08002831 = risk score standard deviation based on the HGDP data.

Unweighted 9-SNP Genetic Risk Score[c]: unweighted 9-SNP genetic risk score equation from Zhou et al (*Zhou* et al, SCI REP. 2014)

Model 1: without adjustment.

Model 2: adjusted by the clinical model from Xie et al (*Xie* et al, AJKD 2018, Epub ahead of print).

Model 3: adjusted by the clinical and pathological model from Xie et al (*Xie* et al, AJKD 2018, Epub ahead of print).

HR, hazard ratio; CI: confidential interval; SNP: single nucleotide polymorphism.

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Table S4 | Reclassification table of models with and without genetic risk score to predict 5-year progression risk.

a) Reclassification table of original clinical risk model alone and combined with genetic risk score

Without genetic risk score	With genetic risk score			Reclassified		Net correctly reclassified
	<5%	5~10%	>10%	Increased risk	Decreased risk	
Individuals without progression						
<5%	0	0	0	9	24	9.55%
5~10%	11	56	9			
>10%	0	13	68			
Individuals with progression						
<5%	0	0	0	2	0	4%
5~10%	0	2	2			
>10%	0	0	46			
Combined						13.55% (4.68%-22.43%)

b) Reclassification table of original clinical-pathological risk model alone and combined with genetic risk score

Without genetic risk score	With genetic risk score			Reclassified		Net correctly reclassified
	<5%	5~10%	>10%	increased risk	Decreased risk	
Individuals without progression						
<5%	0	0	0	0	29	29%
5~10%	0	0	0			
>10%	0	29	71			
Individuals with progression						
<5%	0	0	0	0	0	0
5~10%	0	0	0			
>10%	0	0	43			
Combined						29% (20.11%-37.89%)