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FCRL3 and MTMR3 Gene Polymorphisms Associated with IgA Nephropathy risk in the Chinese Han population

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Objectives:

Immunoglobulin A nephropathy (IgAN) is determined by a combination of multiple genetic and environmental factors, but its etiology and pathogenesis are not well understood. We aim to determine whether variations in *FCRL3* and *MTMR3* correlate with IgAN risk indices in Chinese Han people.

Methods:

Eight single nucleotide polymorphisms (SNPs) of *FCRL3* and *MTMR3* were genotyped, and association analysis was performed. A total of 426 patients with IgAN and 498 healthy individuals, serving as the control group, were recruited for this association study.

Results:

There were significant associations between *FCRL3* rs11264793 (OR = 0.78; 95% CI = 0.63-0.98; $p = 0.029$), rs11264794 (OR = 0.81; 95% CI = 0.67-0.98; $p = 0.026$) and rs7522061 (OR = 0.79; 95% CI = 0.65-0.95; $p = 0.012$) and decreased risk of IgAN according to allele model results. Under genetic models, *FCRL3* and *MTMR3* were associated with the risk of IgAN. Interestingly, *FCRL3* reduced the IgAN susceptibility only in females, while *MTMR3* was a risk factor for IgAN only in males. In addition, *FCRL3* rs11264793 and rs7522061 had protective effects regarding to different disease grades. Moreover, the haplotypes ACC ($p = 0.02$) and CTC ($p = 0.017$) of LD block rs11264794/rs7522061/rs11264799 in the *FCRL3* gene were significantly associated with a decreased risk of IgAN.

Conclusions:

We suggest that gene polymorphisms in *FCRL3* and *MTMR3* may remarkably influence IgAN susceptibility in Chinese Han populations. These findings may be useful in the development of early prognostics for IgAN.

Table 4 Stratification analysis of the association of FCRL3 and MTMR3 polymorphisms with IgA nephropathy under additive genetic mode

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	rs11264793(FCRL3)		rs7522061(FCRL3)		rs11264794(FCRL3)		rs5763688(MTMR3)	
	OR(95%CI)	P [†]	OR(95%CI)	P [†]	OR(95%CI)	P [†]	OR(95%CI)	P [†]
Grade (Lee'sIII)								
< III	0.67(0.47-0.95)	0.023*	0.75(0.57-0.98)	0.056	0.77(0.59-1.01)	0.062	1.07(0.80-1.43)	0.639
≥ III	0.81(0.63-1.06)	0.120	0.62(0.40-0.95)	0.027*	0.84(0.68-1.03)	0.098	1.24(0.99-1.56)	0.164
Sex								
Male	0.84(0.63-1.11)	0.226	0.88(0.69-1.11)	0.267	0.91(0.72-1.15)	0.440	1.37(1.07-1.76)	0.014*
Female	0.64(0.43-0.94)	0.024*	0.66(0.48-0.90)	0.010*	0.65(0.48-0.89)	0.008*	0.90(0.64-1.26)	0.535
Age								
< 32	0.57(0.41-0.81)	0.002*	0.61(0.46-0.81)	0.0006*	0.61(0.46-0.82)	0.0009*	1.20(0.90-1.61)	0.214
≥ 32	1.04(0.74-1.45)	0.832	0.94(0.72-1.24)	0.667	0.93(0.71-1.22)	0.616	1.18(0.87-1.59)	0.298

[†] *p* values were calculated by unconditional logistic regression with adjustment for age and gender.
 **p* < 0.05 indicates statistical significance.

Table 5 Haplotype frequencies of SNPs in the FCRL3 gene and the association with IgAN risk

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Chromosome	Haplotype	Freq (case)	Freq (control)	OR(95%CI)	<i>p</i> [†]
chr1	rs11264794 rs7522061 rs11264799				
	ACT	0.192	0.205	0.92(0.73-1.16)	0.468
	ACC	0.158	0.198	0.75(0.59-0.96)	0.028*
	ATC	0.060	0.061	1.00(0.69-1.47)	0.977
	CTC	0.415	0.471	0.80(0.66-0.96)	0.017*

[†] *p* values were calculated by unconditional logistic regression with adjustment for age and gender.
 * *p* < 0.05 indicates statistical significance.