Association of FOS-Like Antigen 1 Promoter Polymorphism with Podocyte Foot Process Effacement in Immunoglobulin A Nephropathy Patients

Hae Jeong Park,¹ Jong Woo Kim,¹ Byoung-Soo Cho,² and Joo-Ho Chung^{1*}

¹Kohwang Medical Research Institute, School of Medicine, Kyung Hee University, Seoul, Republic of Korea

²Department of Pediatrics, East West Kidney Diseases Research Institute, School of Medicine, Kyung Hee University, Seoul, Republic of Korea

Background: FOS has been implicated in the progression of renal disease including IgAN. In this study, we investigated whether polymorphisms of FOS family genes [*FOS*, *FOSB*, FOS-like antigen 1 (*FOSL1*), and *FOSL2*] were associated with immunoglobulin A nephropathy (IgAN) and the clinical phenotypes of IgAN patients. **Methods:** We genotyped single nucleotide polymorphisms (SNPs) of FOS family genes (rs2239615 and rs7101 for *FOS*, rs12373539 and rs2282695 for *FOSB*, rs637571 for *FOSL1*, and rs925255 for *FOSL2*) using direct sequencing in 198 IgAN patients and 290 control subjects. **Results:** No SNPs were associated with

IgAN; however, in the analysis of clinical phenotypes, we found that rs637571 of *FOSL1* was associated with podocyte foot process effacement of IgAN in additive (CT vs. TT vs. CC, $P = 0.0031$, OR = 2.08, 95% CI = 1.27–3.40) and dominant models (CT/TT vs. CC, $P = 0.0034$, OR = 2.50, 95% CI = 1.35–4.64). The frequency of genotypes containing the T allele was increased in IgAN patients with podocyte foot process effacement, compared to those without podocyte foot process effacement. **Conclusion:** These results suggest that *FOSL1* may be related to IgAN severity. J. Clin. Lab. Anal. 28:391–397, 2014. © 2014 Wiley Periodicals, Inc.

Key words: immunoglobulin A nephropathy; FOS; FOS-like antigen 1; single nucleotide polymorphism; podocyte foot process effacement

INTRODUCTION

Immunoglobulin A nephropathy (IgAN) is the most common form of glomerulonephritis in children and adolescents, leading to end-stage renal failure in >20% of patients after several decades (1, 2). It is characterized pathologically by macroscopic or microscopic hematuria, mesangial IgA deposits, proliferation of mesangial cells, and increased synthesis of extracellular matrix (1). The most common features in renal biopsies of IgAN patients are mesangial expansion and proliferation, but a great variety of both glomerular and interstitial lesions has been observed, with some patients showing only mild mesangial proliferation and others showing marked glomerular and interstitial damage (3). In addition, numerous studies have suggested that the presence of necrotizing glomerular lesions in primary IgAN indicates a worse prognosis, probably because these can recur and accumulate, leading to progression of the disease (4, 5).

Proto-oncogenes, cellular homologues of oncogenes, have been implicated in the control of cell proliferation and differentiation (6). Several studies have shown that some proto-oncogenes are overexpressed in the glomeruli of patients with IgAN. Indeed, increased protein expression of proto-oncogenes such as FOS, MYC, and TP53 were shown in the glomeruli of patients with IgAN as well as lupus nephritis, and focal glomerular sclerosis (7). An increase in the expression of the *FOS* gene was also shown in biopsies from IgAN patients with necrotizing

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*Correspondence to: Joo-Ho Chung, Kohwang Medical Research Institute, School of Medicine, Kyung Hee University, 26 Kyungheedaero, Dongdaemun-gu, Seoul 130-701, Republic of Korea. E-mail: hjpark17@gmail.com

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glomerular lesions (8). Moreover, the levels of mRNA expression of *MYC*, *RAF*, *FOS*, and *JUN* were elevated in the peripheral mononuclear cells of patients with IgAN compared to normal individuals, and the levels positively correlated with renal histological changes and the magnitude of proteinuria (9).

Considering these previous reports, we speculate that proto-oncogenes may play a role in the pathophysiology of IgAN and may be involved in its progression. However, to our knowledge, there have not been any studies of the possible genetic association of proto-oncogenes with IgAN. In this study, we selected single nucleotide polymorphisms (SNPs) of several proto-oncogenes such as *MYC* (rs4645943), *TP53* (rs17886760), and *JUN* (rs2760501), and investigated a genetic association between these SNPs, and childhood IgAN and its clinical phenotypes. However, we did not find any association of SNPs in *MYC*, *TP53* and *JUN* (data not shown). We also assessed an association between FOS family genes [*FOS*, *FOSB*, FOS-like antigen 1 (*FOSL1*), and *FOSL2*] and IgAN. Interestingly, we found that SNP of *FOSL1* was associated with podocyte foot process effacement of IgAN.

METHODS

Subjects

A total of 198 IgAN patients (mean age $\pm$ SD, 12.6 $\pm$ 5.2 years; male/female, 117/81) and 290 control subjects (mean age, 37.5 $\pm$ 13.5 years; male/female, 158/132) were enrolled in this study. Demographic and clinical findings of IgAN patients are shown in Table 1. Each IgAN patient was checked by two pediatricians. IgAN patients with (a) unexplained prolonged isolated hematuria or proteinuria longer than 12 mo, (b) concomitant hematuria and proteinuria longer than 3 mo, (c) a second episode of gross hematuria with decreased serum C3 and C4 levels, or (d) decreased renal function were included in this study, and a renal biopsy was performed in all IgAN patients. To determine the relationship between FOS family gene polymorphisms and clinical phenotypes, IgAN patients were divided into subgroups according to the presence of gross hematuria as an initial symptom of IgAN, the presence of advanced disease markers (interstitial fibrosis, tubular atrophy, or global sclerosis), the presence of podocyte foot process effacement, the degree of mesangial proliferation (mild group, subjects with normal-to-mild focal mesangial proliferation; advanced group, those with mild diffuse to severe diffuse mesangial proliferation), and proteinuria level at kidney biopsy (≤ 4 or >4 mg/m²/h). In addition, IgAN patients were pathologically classified by the modified H. S. Lee's histological grading system (10) as follows: grade I, normal or

TABLE 1. Demographic Characteristics of the Study Subjects

	IgAN (n = 198)	Control (n = 290)
Number of subject (male/female)	117/81	158/132
Age (mean $\pm$ SD, years)	12.6 $\pm$ 5.2	37.5 $\pm$ 13.5
Gross hematuria ^a		
-/+	160/38	
Advanced disease marker ^b		
-/+	178/20	
Podocyte foot process effacement		
-/+	125/73	
Mesangial proliferation ^c		
Mild/advanced	129/69	
24-h proteinuria (mean $\pm$ SD, mg/m ² /h) ^d		
≤ 4	107 (1.8 $\pm$ 0.9)	
> 4	91 (28.4 $\pm$ 45.6)	
Pathological grading ^e		
I/II/III/IV/V	124/57/15/2/0	

^aGross hematuria develops as the first symptom of IgAN.

^bAdvanced disease markers mean interstitial fibrosis, tubular atrophy, or global sclerosis at renal biopsy.

^cMesangial proliferation was assessed according to the degree of mesangial proliferation at renal biopsy: mild (normal to mild focal mesangial proliferation) vs. advanced (mild diffuse to severe diffuse mesangial proliferation).

^dProteinuria means the amount of proteinuria that developed at the time of kidney biopsy.

^ePathological grading was determined by the modified H. S. Lee's histological grading system as follows: grade I, normal or focal mesangial cell proliferation; grade II, diffuse mesangial cell proliferation or $<25\%$ of glomeruli with crescent (Cr)/segmental sclerosis (SS)/global sclerosis (GS); grade III, 25–49% of glomeruli with Cr/SS/GS; grade IV, 50–75% of glomeruli with Cr/SS/GS; grade V, $>75\%$ of glomeruli with Cr/SS/GS.

IgAN, immunoglobulin A nephropathy; SD, standard deviation; n, number.

focal mesangial cell proliferation; grade II, diffuse mesangial cell proliferation, or $<25\%$ of glomeruli with crescent (Cr)/segmental sclerosis (SS)/global sclerosis (GS); grade III, 25–49% of glomeruli with Cr/SS/GS; grade IV, 50–75% of glomeruli with Cr/SS/GS; grade V, $>75\%$ of glomeruli with Cr/SS/GS. And then, they were divided into pathologically mild (grade I–II) and advanced (grade III–IV) disease groups. Healthy adults were used as the control group due to difficulty in obtaining samples from healthy children (11, 12). The control group was recruited from subjects visiting the hospital for routine health checkups. Healthy subjects without a history of IgAN symptoms or any other diseases were used as the control group.

All IgAN patients and control subjects were recruited from the Kyung Hee Medical Center in Seoul, Republic of Korea and were of Korean background. The present study was conducted in accordance with the guidelines of the Helsinki Declaration and was approved by the Ethics Review Committee of the Medical Research Institute, Kyung Hee University Medical Center. Written informed consent

was obtained from the parents or guardians of IgAN patients and from control subjects.

SNP selection and genotyping

SNPs located in the promoter (within -1,000 bp from the transcriptional start sites) or exon [5'-untranslated region (UTR), coding region, and 3'UTR] of the *FOS*, *FOSB*, *FOSL1*, and *FOSL2* genes were selected from the National Center for Biotechnology Information SNP database (<http://www.ncbi.nlm.nih.gov/SNP>, BUILD 137). We excluded SNPs without data on genotype frequency, and those with a minor allele frequency (MAF) <0.1 in Chinese and Japanese populations. Finally, we selected six SNPs [rs2239615 (+71A/T) and rs7101 (+146T/C) for *FOS*; rs12373539 (-158G/A) and rs2282695 (Ala39Ala) for *FOSB*; rs637571 (Gln77Gln) for *FOSL1*; rs925255 (-985G/A) for *FOSL2*]. DNA was isolated from a peripheral blood sample using the DNA Isolation Kit for blood (Roche, IN, USA). SNP genotyping was conducted using direct sequencing using the specific primers for rs2239615 (sense: 5'-ATGCTCACGAGATTAGGACACG-3'; anti-sense: 5'-CGGGTGAGTGGTAGTAAGAGA-3'), rs7101 (sense: 5'-CCCGTGACGTTTACACTCATT-3'; anti-sense: 5'-GCGGGTGAGTGGTAGTAAGAGA-3'), rs12373539 (sense: 5'-TGACGTCATTGCTAGGATACCA-3'; anti-sense: 5'-GGCCGTAGCTCTGAGTCTTATG-3'), rs2282695 (sense: 5'-GACTTGCACCTTACTTCCCCAAC-3'; anti-sense: 5'-TCTCAGATCTAGGGTTCTGATG-3'), rs637571 (sense: 5'-GACTTGCACCTTACTTCCCCAAC-3'; anti-sense: 5'-TCTCAGATCTAGGGTTCTGATG-3'), and rs925255 (sense: 5'-CCTGCTCTAAGGTCTGTGCTCT-3'; anti-sense: 5'-CTACCGGTTCCCTTTTGT TTT-3'). The PCR products were sequenced using an ABI PRISM 3730XL analyzer (PE Applied Biosystems, Foster City, CA, USA). Sequence data were analyzed using SeqManII software (DNASTAR Inc., Madison, WI, USA).

Statistical analysis

SNPStats (<http://bioinfo.iconcologia.net/index.php>) and SPSS 18.0 software (SPSS Inc., Chicago, IL, USA) were used to analyze the genetic data and the Hardy-Weinberg equilibrium (HWE). The associations between the genotypes of SNPs and IgAN, as well as any associations between the genotypes of SNPs and IgAN subgroups were estimated by computing the odds ratios (ORs) and their 95% confidence intervals (CIs) with logistic regression analysis, controlling for gender as a co-variable. In the logistic regression analysis for each SNP, models assuming additive inheritance, dominant inheritance, or recessive inheritance were used. To avoid chance

findings due to multiple testing, a Bonferroni correction was applied by lowering the significance levels to $P = 0.05/6$ for the six SNPs.

RESULTS

The six SNPs analyzed in this study were polymorphic, and the genotype distributions of the SNPs were in HWE ($P > 0.05$; data not shown). We calculated the power of the sample size to verify our data using a genetic power calculator (<http://pnu.mgh.harvard.edu/~purcell/gpc/cc2.html>). Considering a two-fold genotype relative risk, the sample powers of the SNPs were 0.965 (rs2239615, number of effective samples for 80% power = 113), 0.966 (rs7101, $n = 112$), 0.955 (rs12373539, $n = 120$), 0.951 (rs2282695, $n = 123$), 0.876 (rs637571, $n = 159$), and 0.877 (rs925255, $n = 161$) ($\alpha = 0.05$). We therefore had statistical confidence in our results.

As shown in Table 2, no SNPs of the FOS family genes were associated with IgAN; however, in the analysis according to the clinical phenotypes of IgAN (gross hematuria, advanced disease markers, podocyte foot process effacement, mesangial proliferation, proteinuria level, and pathological grading), we found significant associations between *FOSL1* and podocyte foot process effacement. Mean age of patients without podocyte foot process effacement (male/female, 74/51) and patients with podocyte foot process effacement (male/female, 43/30) was 12.5 ± 5.2 and 12.7 ± 5.1 years, respectively (Supporting Information Table 1). As shown in Table 3, in an analysis according to the absence or presence of podocyte foot process effacement, rs637571 of *FOSL1* was associated with podocyte foot process effacement in the additive (CT vs. TT vs. CC) and dominant models (CT/TT vs. CC). In the additive model, the frequencies of the CT (36.6%) and TT genotypes (9.9%) were increased in the patients with podocyte foot process effacement compared to those without podocyte foot process effacement (21.8% for CT; 4% for TT) ($P = 0.0031$, OR = 2.08, 95% CI = 1.27–3.40). In the dominant model, the frequency of the genotype containing the T allele (CT/TT, 46.5%) was higher in the patients with podocyte foot process effacement than in those without podocyte foot process effacement (25.8%) ($P = 0.0034$, OR = 2.50, 95% CI = 1.35–4.64). The frequencies of the genotypes containing the T allele were increased in IgAN patients with podocyte foot process effacement, compared to those without podocyte foot process effacement. These results remained significant after Bonferroni correction.

In the analysis according to other clinical phenotypes, we were not able to find any association of polymorphisms in the FOS family genes (data not shown).

TABLE 2. Multiple Logistic Regression Analysis of Polymorphisms of the FOS Family Genes between Immunoglobulin A Nephropathy Patients and Control Subjects

Gene	SNP	Model	Genotype	Control <i>n</i> (%)	IgAN <i>n</i> (%)	OR (95% CI)	<i>P</i>
<i>FOS</i>	rs2239615 +71A/T (5'UTR)	Additive	AA	88 (31.1)	63 (31.8)	1	0.36
			AT	150 (53.0)	90 (45.5)	-	
			TT	45 (15.9)	45 (22.7)	1.13 (0.87–1.47)	
		Dominant	AA	88 (31.1)	63 (31.8)	1	0.84
			AT/TT	195 (68.9)	135 (68.2)	0.96 (0.65–1.42)	
		Recessive	AA/AT	238 (84.1)	153 (77.3)	1	0.063
			TT	45 (15.9)	45 (22.7)	1.55 (0.98–2.46)	
	rs7101 +146T/C (5'UTR)	Additive	TT	89 (30.7)	63 (31.8)	1	0.52
			TC	151 (52.1)	90 (45.5)	-	
			CC	50 (17.2)	45 (22.7)	1.09 (0.84–1.41)	
		Dominant	TT	89 (30.7)	63 (31.8)	1	0.77
			TC/CC	201 (69.3)	135 (68.2)	0.94 (0.64–1.39)	
		Recessive	TT/TC	240 (82.8)	153 (77.3)	1	0.14
<i>FOSB</i>	rs12373539 –158G/A (Promoter)	Additive	GG	134 (46.2)	85 (42.9)	1	0.32
			GA	126 (43.5)	87 (43.9)	-	
			AA	30 (10.3)	26 (13.1)	1.15 (0.88–1.50)	
		Dominant	GG	134 (46.2)	85 (42.9)	1	0.46
			AG/AA	156 (53.8)	113 (57.1)	1.15 (0.80–1.65)	
		Recessive	GG/AG	260 (89.7)	172 (86.9)	1	0.35
	rs2282695 Ala39Ala (Synonymous)	Additive	AA	30 (10.3)	26 (13.1)	1.31 (0.75–2.29)	
			CC	135 (46.5)	92 (46.5)	1	0.84
			CG	124 (42.8)	82 (41.4)	-	
		Dominant	GG	31 (10.7)	24 (12.1)	1.03 (0.79–1.34)	
			CC	135 (46.5)	92 (46.5)	1	0.98
		Recessive	CG/GG	155 (53.5)	106 (53.5)	0.99 (0.69–1.43)	
<i>FOSL1</i>	rs637571 Gln77Gln (Synonymous)	Additive	CC	196 (67.6)	130 (66.7)	1	0.64
			CT	84 (29.0)	53 (27.2)	-	
			TT	10 (3.5)	12 (6.2)	1.11 (0.81–1.52)	
			TT	10 (3.5)	12 (6.2)	1.75 (0.74–4.17)	
		Dominant	CC	196 (67.6)	130 (66.7)	1	0.83
			CT/TT	94 (32.4)	65 (33.3)	1.04 (0.71–1.54)	
		Recessive	CC/CT	280 (96.5)	183 (93.8)	1	0.20
			TT	10 (3.5)	12 (6.2)	1.75 (0.74–4.17)	
<i>FOSL2</i>	rs925255 –985G/A (Promoter)	Additive	GG	189 (65.2)	126 (63.6)	1	0.87
			GA	87 (30.0)	67 (33.8)	-	
			AA	14 (4.8)	5 (2.5)	0.97 (0.71–1.34)	
			AA	14 (4.8)	5 (2.5)	0.51 (0.18–1.45)	
		Dominant	GG	189 (65.2)	126 (63.6)	1	0.74
			GA/AA	101 (34.8)	72 (36.4)	1.06 (0.73–1.55)	
		Recessive	GG/GA	276 (95.2)	193 (97.5)	1	0.19
			AA	14 (4.8)	5 (2.5)	0.51 (0.18–1.45)	

DISCUSSION

The FOS family consists of four members: FOS, FOSB, FOSL1, and FOSL2. The protein encoded by these genes are part of the activator protein-1 (AP-1) transcription factor, and as such they have been shown to participate in the molecular mechanisms of cell proliferation, differentiation, apoptosis, and transformation (13). Moreover, the deregulation of these proteins has been linked to a variety of pathological conditions, including immunological, skeletal, and neurological defects, as well as oncogenic transformation and tumor progression (13).

A large number of studies have suggested that genetic factors contributed to the development and progression of IgAN (14). Indeed, candidate gene approaches have demonstrated that a wide variety of gene polymorphisms including major histocompatibility complex (*MHC*) class II, T-cell receptor (*TCR*), and angiotensin-converting enzyme (*ACE*) were associated with onset and/or progression of IgAN (14). In addition, recent studies showed that polymorphisms of the atherosclerotic disease-related genes such as glycoprotein Ia (*GPIa*), intercellular adhesion molecule 1 (*ICAM1*), and 5-methyltetrahydrofolate-

TABLE 3. Multiple Logistic Regression Analysis of Polymorphisms of the FOS Family Genes in Immunoglobulin A Nephropathy Patients with or without Podocyte Foot Process Effacement

Gene	SNP	Model	Genotype	Podocyte foot process effacement		OR (95% CI)	P
				– n (%)	+ n (%)		
<i>FOS</i>	rs2239615 +71A/T (5'UTR)	Additive	AA	38 (30.4)	25 (34.2)	1	
			AT	56 (44.8)	34 (46.6)	-	
			TT	31 (24.8)	14 (19.2)	0.84 (0.56–1.25)	0.39
		Dominant	AA	38 (30.4)	25 (34.2)	1	
			AT/TT	87 (69.6)	48 (65.8)	0.84 (0.45–1.57)	0.59
		Recessive	AA/AT	94 (75.2)	59 (80.8)	1	
	rs7101 +146T/C (5'UTR)	Additive	TT	31 (24.8)	14 (19.2)	0.72 (0.35–1.47)	0.36
			TC	38 (30.4)	25 (34.2)	1	
			CC	56 (44.8)	34 (46.6)	-	
		Dominant	TT	31 (24.8)	14 (19.2)	0.84 (0.56–1.25)	0.39
			TC/CC	38 (30.4)	25 (34.2)	1	
		Recessive	TT/TC	87 (69.6)	48 (65.8)	0.84 (0.45–1.57)	0.59
<i>FOSB</i>	rs12373539 –158G/A (Promoter)	Additive	CC	94 (75.2)	59 (80.8)	1	
			CG	31 (24.8)	14 (19.2)	0.72 (0.35–1.47)	0.36
			GG	57 (45.6)	28 (38.4)	1	
		Dominant	GA	52 (41.6)	35 (48.0)	-	
			AA	16 (12.8)	10 (13.7)	1.19 (0.78–1.81)	0.43
		Recessive	GG	57 (45.6)	28 (38.4)	1	
	rs2282695 Ala39Ala (Synonymous)	Additive	AG/AA	68 (54.4)	45 (61.6)	1.35 (0.74–2.43)	0.32
			GG/AG	109 (87.2)	63 (86.3)	1	
			AA	16 (12.8)	10 (13.7)	1.08 (0.46–2.53)	0.86
		Dominant	CC	55 (44.0)	37 (50.7)	1	
			CG/GG	70 (56.0)	36 (49.3)	0.76 (0.43–1.37)	0.36
		Recessive	CC/CG	109 (87.2)	65 (89.0)	1	
<i>FOSL1</i>	rs637571 Gln77Gln (Synonymous)	Additive	GG	16 (12.8)	8 (11.0)	0.84 (0.34–2.09)	0.71
			CC	92 (74.2)	38 (53.5)	1	
			CT	27 (21.8)	26 (36.6)	-	
		Dominant	TT	5 (4.0)	7 (9.9)	2.08 (1.27–3.40)	0.0031
			CC	92 (74.2)	38 (53.5)	1	
		Recessive	CT/TT	32 (25.8)	33 (46.5)	2.50 (1.35–4.64)	0.0034
<i>FOSL2</i>	rs925255 –985G/A (Promoter)	Additive	CC/CT	119 (96.0)	64 (90.1)	1	
			TT	5 (4.0)	7 (9.9)	2.76 (0.81–9.39)	0.10
			GG	77 (61.6)	49 (67.1)	1	
		Dominant	GA	45 (36.0)	22 (30.1)	-	
			AA	3 (2.4)	2 (2.7)	0.84 (0.48–1.44)	0.52
		Recessive	GG	77 (61.6)	49 (67.1)	1	
			GA/AA	48 (38.4)	24 (32.9)	0.79 (0.43–1.45)	0.44
			GG/GA	122 (97.6)	71 (97.3)	1	
			AA	3 (2.4)	2 (2.7)	1.17 (0.19–7.23)	0.87

Bold characters represent statistically significant values ($P < 0.05/6$).

homocysteine methyltransferase (*MTR*) were associated with the development and progression of IgAN (15, 16). They postulated that it may be due to the involvement of atherosclerotic metabolic factors such as obesity, fasting triglyceride, insulin resistance, and uric acid in renal prognosis of IgAN (16), and contribution of oxidative stress, which plays an important role in the atherosclerotic diseases, to the pathophysiology of IgAN (15, 17).

In IgAN, previous studies have reported the overexpression of FOS, which is involved in the inflammation and pathogenic changes in atherosclerosis, and has been described as a candidate marker of atherosclerosis, showing strong expression in the leukocytes of patients with atherosclerosis (18). Takemura et al. (7) showed increased protein expression of FOS with MYC, and TP53 in the glomeruli of patients with IgAN, lupus nephritis,

and focal glomerular sclerosis compared to patients with minimal change nephrotic syndrome and normal specimens, suggesting that the expression of these genes was associated with mesangial proliferation and matrix expansion in proliferative types of glomerulonephritis and in focal glomerular sclerosis. Rastaldi et al. (8) also showed increased FOS expression with TGFB and ET1 in biopsies of IgAN patients with necrotizing glomerular lesions compared to those without the necrotizing lesions and normal subjects. In addition, the expression of these genes was not different between IgAN patients without necrotizing glomerular lesions and normal subjects (8). Thus, the role of FOS, TGFB, and ET1 was suggested to be involved in glomerular damage leading to further progression of the disease (8). Given these reports, we postulated that FOS and other FOS family genes may be involved in the severity of IgAN rather than incidence of IgAN by impacting the proliferation of mesangial cells and glomerular damage. In our study, FOS family genes were not associated with IgAN. Interestingly, we found that rs637571 of *FOSL1* was associated with podocyte foot process effacement, although FOS family genes were not associated with other symptoms of IgAN. In particular, the genotypes containing the T allele of rs637571 were associated with an increased risk of podocyte foot process effacement in IgAN patients.

Podocytes are specialized epithelial cells located on the outer surface of the glomerular basement membrane, and foot process denotes their cell processes. Foot processes are a major component of the glomerular filtration barrier to protein along with the endothelial cell and glomerular basement membrane. The effacement of foot process is frequently observed in glomerulonephritides presenting with proteinuria (19–21), and is considered a sign of glomerular injury (1, 3, 19). In our study, we found that the frequency of the genotypes containing the T allele of rs637571 in *FOSL1* was increased in IgAN patients with podocyte foot process effacement. This result indicated that the T allele of rs637571 in *FOSL1* may contribute to the development of podocyte foot process effacement in IgAN and thus glomerular injury. Further research is needed to investigate how FOS family genes and their polymorphisms affect podocyte foot process effacement and glomerular damage in IgAN. In addition, because of the relatively small number of subjects, our findings are preliminary and need to be validated in further studies with larger sample sizes.

In conclusion, we found that *FOSL1* was significantly associated with podocyte foot process effacement in IgAN patients. In particular, the genotypes containing the T allele of rs637571 were associated with a higher risk of podocyte foot process effacement in IgAN patients. These results suggested that the T allele of rs637571 may be related to IgAN severity.

CONFLICT OF INTEREST

None declared.

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