Original Paper

Interleukin-2 and Interleukin-8 Gene Polymorphisms and Acquired Aplastic Anemia Risk in a Chinese Population

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Key Words

Acquired aplastic anemia • Interleukin-2 • Interleukin-8 • Polymorphism • Transcription

Abstract

Background/Aims: Cytokines IL-2 and IL-8 both participate in immune regulation. However, the relationship between polymorphisms in these two cytokines and the risk of acquired aplastic anemia (acquired AA) has not been explored. **Methods:** We selected five SNPs including rs11575812, rs2069772 and rs2069762 of IL-2, rs2227306 and rs2227543 of IL-8. SNaPshot genotyping was used to test the genotypes of IL-2 and IL-8 polymorphisms in a population of 101 acquired AA patients and 165 healthy controls. **Results:** The rs2069762 G allele appeared to be a protective mutation, but no significant differences were found in other four SNPs. We also found that rs2069762 had an impact on the transcriptional regulation. **Conclusions:** It could be assumed that the rs2069762 polymorphism might reduce the risk of acquired aplastic anemia, while the remaining four SNPs might not contribute to susceptibility to acquired AA in a Chinese population.

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Introduction

Acquired aplastic anemia (AA) is a rare hematologic disease characterized by pancytopenia in peripheral blood (PB) and bone marrow (BM) hypoplasia [1]. The main clinical manifestations of acquired AA patients are anemia, hemorrhage and infection [2]. Although the pathogenesis of acquired AA is complicated and has not been fully understood, the immune-mediated destruction of hematopoietic stem cells (HSCs) is believed to be the main nosogenesis [3]. Recent studies suggest that aberrant T cell immune homeostasis plays

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a key role in the pathogenesis of acquired AA [4]. Abnormal activation of Th1 T-cell causes excessive production of hematopoietic negative regulatory cytokines, such as interleukin-2 (IL-2), interferon- γ (IFN- γ), IL-8, tumor necrosis factor- α (TNF- α) and so on. These cytokines contribute to inhibiting hematopoiesis, which is correlated with disease activity [5, 6].

As an important immunoregulatory cytokine, IL-2 is a autocrine and paracrine molecule, which is produced mainly by activated CD4⁺ T-cells, naive CD8⁺ T-cells and dendritic cells [7]. It was reported that IL-2 could stimulate the activation, proliferation and differentiation of many immune cells including natural killer (NK), B and T-cells [8]. So, as a T-cell growth factor, IL-2 is mainly produced by active T cells and in turn affects the proliferation of T-cells. IL-2 has pleiotropic effects on the regulatory function of immune system [9]. Another hematopoietic negative regulatory factor, Interleukin-8, is an angiogenic chemokine, which can be produced by different cell types, such as neutrophils, macrophages, epithelial cells and endothelial cells [10]. Interleukin-8 is an effective inhibitor of myelopoiesis [6]. According to previous studies, levels of IL-2 and IL-8 were both evidently increased in the bone marrow and peripheral blood of acquired AA patients when compared to their healthy controls. So we propose that the abnormality of these two cytokines might cause immune dysfunction and lead to the suppression of haemopoiesis, resulting in the occurrence of acquired aplastic anemia [6, 11].

It is well known that single nucleotide polymorphisms (SNPs) may influence the individual susceptibility to diseases. Polymorphic variants in IL-2 region have already been discovered to be related to a number of autoimmune diseases, such as type 1 diabetes (T1D) [12], rheumatoid and juvenile idiopathic arthritis [13, 14], multiple sclerosis [15], psoriasis [16], inflammatory bowel disease and systemic lupus erythematosus (SLE) [17-19]. In addition, some previous studies have revealed that the IL-8 gene polymorphisms are linked to higher risk of osteoarthritis, osteosarcoma, oral and gastric cancer [20-23]. However, little was known about the association between these two cytokine genes polymorphisms and the risk of acquired AA.

In our study, we selected the SNPs whose minor allele frequency (MAF) value were greater than 5% in the Chinese population and located in potential functional regions of IL-2 and IL-8. According to these criteria, we identified three SNPs of IL-2 (rs11575812, rs2069772 and rs2069762) and two SNPs of IL-8 (rs2227306 and rs2227543) using Pubmed and the Hapmap database. Besides, the rs2069762 in the IL-2 promoter, which had already been researched in other autoimmune diseases studies [12-19], was also included in our study. Consequently, a case-control study was performed to evaluate the relevance between these five SNPs and the risk of acquired AA in a Chinese population.

Materials and Methods

Study subject

Our study subjects contain 101 acquired AA patients and 165 healthy controls, who were recruited from Children's Hospital of Nanjing Medical University, the First Affiliated Hospital of Nanjing Medical University, the Affiliated Soochow Children's Hospital of Soochow University, the First Hospital of Jilin University and the First Affiliated Hospital, Zhejiang Chinese Medical University from July 2014 to 2015 November. The mean age ($\pm$ SD) of these cases was 24.7 ± 21.1 years. Patients were diagnosed with acquired AA by biopsy and peripheral blood (PB) cell count. Their PB cell count involved at least two lineages, values have to lower than $<100\text{g/L}$ for hemoglobin, than $1.5 \times 10^9/\text{L}$ for neutrophils and than $50 \times 10^9/\text{L}$ for platelets. Bone marrow presented with reduced hematopoietic cells while major dysplastic signs and marrow fibrosis were ruled out. Combined with detailed physical examination, radiography of bone and related gene detection, we excluded Fanconi anemia and dyskeratosis congenital. These controls, with a mean age ($\pm$ SD) of 27.2 ± 21.2 years, had no blood disease or cancer history. All controls were matched to cases in terms of gender and age (± 16 years) and have no genetic relationship with cases. Our research program was approved by the Institutional Review Board of Children's Hospital of Nanjing Medical University.

Genotyping

Genomic DNA was extracted from peripheral blood of every study subject by using the standard protocols of Relax Gene Blood DNA System (TIANGEN, Beijing, China). Blood samples of patients were all collected before clinical treatments. The DNA samples were stored at -20°C until used. Five SNPs were detected in the DNA samples from 101 cases and 165 controls by using the method of SNaPshot.

Statistical analysis

To identify possible selection bias and genotyping errors, Hardy-Weinberg equilibrium of the genotype distribution among control subjects was estimated using a goodness of fit χ^2 test. The crude and adjusted odds ratios (OR) for risk of acquired AA and 95% confidence intervals (CI) were calculated by univariate and multivariate logistic regression analyses. The multivariate adjustment included age (± 16 years) and gender. All tests were two-sided and P-value < 0.05 was regarded as statistically significant. Statistical analyses were carried out by Statistical Analysis System software (version 9.2; SAS Institute, Cary, NC, USA).

Functional prediction

Bioinformatics tools of SNPinfo (<http://snpinf.niehs.nih.gov/snpinfo/snpfunc.php>) and F-SNP (<http://compbio.cs.queensu.ca/F-SNP/>) were used to predict the potential functions of significant SNPs.

Results

Correlation analysis results

The frequency distributions of the selected demographic variables of acquired AA patients and controls are shown in Table 1. There were no statistical differences in age (P = 0.502) and sex (P = 0.441) between the case and control groups.

Table 2 showed the primary information and allele frequencies of these selected SNPs. The allele frequencies of these five polymorphisms conformed to Hardy-Weinberg equilibrium among the control group (0.790, 0.624, 0.258, 0.394 and 0.423, respectively). Allele analysis of rs2069762 revealed different distributions between cases and controls (P = 0.022).

The genotypic distributions of the selected five SNPs are summarized in Table 3. In general, one SNP rs2069762 demonstrated different distributions between the case and

Table 1. Frequency distributions of age and gender in Chinese acquired AA cases and controls.*Two-sided chi-square test for frequency distributions of age and gender between cases and controls

Variables	Cases(n = 101)		Controls (n = 165)		p*
	n	%	n	%	
Age (years)					
≤16	44	43.56	64	38.79	0.502
>16	57	56.44	101	61.21	
Gender					
Male	57	56.44	100	60.61	0.441
Female	44	43.56	65	39.39	

Table 2. Primary information of genotyped SNPs. ^aTwo-sided χ^2 test for allele frequencies between cases and controls. ^bP value for Hardy-Weinberg equilibrium in the control group

SNP	Base change	Gene name	Chr	Minor allele frequencies			P ^a	Hardy-Weinberg equilibrium ^b
				Database	cases	controls		
rs11575812	T>C	IL-2	4	0.102	0.114	0.088	0.327	0.790
rs2069772	A>G	IL-2	4	0.105	0.109	0.096	0.658	0.624
rs2069762	T>G	IL-2	4	0.239	0.287	0.385	0.022	0.258
rs2227306	C>T	IL-8	4	0.367	0.366	0.370	0.938	0.394
rs2227543	C>T	IL-8	4	0.379	0.391	0.385	0.886	0.423

Table 3. Logistic regression analysis was used to evaluate the connection between cytokines polymorphisms and acquired AA risk. [†]The ORs, 95% CIs and P value were calculated after adjusting for age and gender

Genotype	Cases (n = 101)		Controls (n = 165)		OR(95%CI)	Adjusted OR (95%CI) [†]	Adjusted P value
	n	%	n	%			
rs1157582	T/C						
TT	80	79.21	137	83.03	1.00(reference)	1.00(reference)	
CT	19	18.81	27	16.36	1.21(0.63-2.31)	1.2 (0.63 -2.35)	0.555
CC	2	1.98	1	0.61	3.42(0.30 - 38.36)	3.69(0.33 - 41.82)	0.291
CC+CT	21	20.79	28	16.97	1.28(0.68- 2.41)	1.31(0.69- 2.47)	0.408
TT+CT	99	98.02	164	99.39	1.00(reference)	1.00(reference)	
CC	2	1.98	1	0.61	3.31(0.30 -37.00)	3.59 (0.32 -40.53)	0.302
rs2069772	A/G						
AA	82	81.19	134	81.21	1.00(reference)	1.00(reference)	
AG	16	15.84	30	18.18	0.87(0.45-1.70)	0.84(0.43-1.65)	0.613
GG	3	2.97	1	0.61	4.90(0.50-47.91)	5.79(0.58-58.09)	0.136
GG+AG	19	18.81	31	18.79	1.00(0.53-1.89)	0.98(0.52-1.86)	0.961
AA+AG	98	97.03	164	99.39	1.00(reference)	1.00(reference)	
GG	3	2.97	1	0.61	5.02(0.52-48.92)	5.94(0.59-59.47)	0.130
rs2069762	T/G						
TT	51	50.50	59	35.76	1.00(reference)	1.00(reference)	
GT	42	41.58	85	51.52	0.57(0.34-0.97)	0.56 (0.33-0.95)	0.030
GG	8	7.92	21	12.73	0.44(0.18-1.08)	0.46(0.19-1.13)	0.089
GG+GT	50	49.50	106	64.24	0.55(0.33-0.90)	0.54(0.32-0.89)	0.016
TT+GT	93	92.08	144	87.27	1.00(reference)	1.00(reference)	
GG	8	7.92	21	12.73	0.59(0.25-1.39)	0.61(0.26-1.45)	0.267
Rs2227306	C/T						
CC	41	40.59	63	38.18	1.00(reference)	1.00(reference)	
CT	46	45.54	82	49.70	0.86(0.51-1.47)	0.86(0.51-1.48)	0.593
TT	14	13.86	20	12.12	1.07(0.49-2.37)	1.06(0.48-2.33)	0.889
TT+CT	60	59.41	102	61.82	0.90(0.55-1.50)	0.90(0.54-1.50)	0.693
CC+CT	87	86.14	145	87.88	1.00(reference)	1.00(reference)	
TT	14	13.86	20	12.12	1.17(0.56-2.43)	1.147(0.55-2.39)	0.717
Rs2227543	C/T						
CC	38	37.62	60	36.36	1.00(reference)	1.00(reference)	
CT	47	46.53	83	50.30	0.89(0.52-1.54)	0.90(0.52-1.55)	0.705
TT	16	15.84	22	13.33	1.15(0.54-2.46)	1.13(0.52-2.42)	0.761
TT+CT	63	62.38	105	63.64	0.95(0.57-1.58)	0.95(0.57-1.59)	0.840
CC+CT	85	84.16	143	86.67	1.00(reference)	1.00(reference)	
TT	16	15.84	22	13.33	1.22(0.61-2.46)	1.19(0.59-2.41)	0.620

Table 4. Association between rs2069762 polymorphism and selected demographic data. [#]The ORs and 95% CIs were calculated after adjusting for age and gender

	Case n(%)	Control n(%)	TT	GT	GG	#Adjusted OR(95% CI)		
						GT/GG	TT/GT	GG
Sex								
Male	57(56.44)	100(60.61)	1.00 (reference)	0.55(0.27-1.12)	0.55(0.20-1.51)	0.55(0.29- 1.07)	1.00 (reference)	0.73(0.28- 1.90)
Female	44(43.56)	65(39.39)	1.00 (reference)	0.56(0.25- 1.24)	0.21(0.02-2.01)	0.52(0.24-1.14)	1.00 (reference)	0.30(0.03- 2.68)
Age								
≤16	44(43.56)	64(38.79)	1.00 (reference)	0.77(0.34-1.74)	0.48(0.11- 2.12)	0.71(0.32-1.55)	1.00 (reference)	0.55(0.13- 2.28)
>16	57(56.44)	101(61.21)	1.00 (reference)	0.44(0.22-0.89)	0.44(0.14- 1.37)	0.44(0.23-0.86)	1.00 (reference)	0.66(0.22-1.95)

control groups, no significant differences were found in other four SNPs. The rs2069762 G allele appeared to be a protective mutation. According to the results of analysis of rs2069762, the GT (OR=0.56, 95%CI=0.33-0.95, P=0.030) and GT/GG (OR=0.54, 95%CI=0.32-0.89, P=0.016) genotypes showed reduced risk of acquired AA, while the GG (OR=0.46, 95%CI=0.19-1.13, P = 0.089) genotype showed no statistical significance.

Table 5. Comparisons of distributions of the genotypes of five SNPs between NSAA, vSAA and SAA, patients and the controls, which used the logistic regression analysis. *Adjusted for age and gender. Eight patients lack the information of disease severity

Genotype	Controls		Disease severity				OR (95% CI)		*Adjusted OR (95% CI)		*Adjusted P value	
	n=165		NSAA n=24		SAA+vSAA n=69		NSAA	SAA+vSAA	NSAA	SAA+vSAA	NSAA	SAA+ vSAA
rs11575812	n	%	n	%	n	%						
TT	137	83.03	17	70.83	56	81.16	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)		
CT	27	16.36	6	25.00	13	18.84	1.79 (0.65-4.96)	1.18 (0.57-2.45)	1.78 (0.62-5.08)	1.19 (0.56-2.50)	0.283	0.648
CC	1	0.61	1	4.1	0	0	8.06 (0.48-134.8)	-	6.98 (0.41-118.82)	-	0.185	-
CC+CT	28	16.97	7	29.17	13	18.84	2.02 (0.76-5.31)	1.13 (0.54-2.35)	2.01 (0.74-5.45)	1.16 (0.55-2.42)	0.176	0.699
TT+CT	164	99.39	23	95.83	69	100	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)		
CC	1	0.61	1	4.1	0	0	7.13 (0.43-117.96)	-	6.39 (0.38-108.06)	-	0.199	-
rs2069772												
AA	134	81.21	19	79.17	56	81.16	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)		
AG	30	18.18	4	16.67	12	17.39	0.94 (0.29-2.96)	0.95 (0.45-2.00)	0.96 (0.30-3.07)	0.88 (0.41-1.87)	0.953	0.742
GG	1	0.61	1	4.17	1	1.45	7.05 (0.42-117.51)	2.39 (0.14-38.92)	8.12 (0.45-143.98)	3.72 (0.19-70.48)	0.157	0.386
GG+AG	31	18.79	5	20.83	13	18.84	1.13 (0.39-3.28)	1.01 (0.48-2.05)	1.17 (0.40-3.42)	0.94 (0.45-1.96)	0.761	0.889
AA+AG	164	99.39	23	95.83	68	98.55	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)		
GG	1	0.61	1	4.17	1	1.45	7.13 (0.43-117.95)	2.41 (0.14-39.11)	8.17 (0.46-143.88)	3.78 (0.20-71.37)	0.155	0.372
rs2069762												
TT	59	35.76	12	50.00	34	49.28	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)		
GT	85	51.52	1	45.83	29	42.03	0.63 (0.26-1.54)	0.59 (0.32-1.07)	0.65 (0.27-1.60)	0.57 (0.31-1.05)	0.358	0.071
GG	21	12.73	1	4.17	6	8.70	0.23 (0.03-1.91)	0.49 (0.18-1.35)	0.22 (0.02-1.83)	0.56 (0.20-1.54)	0.162	0.261
GG+GT	106	64.24	12	50.00	35	50.72	0.55 (0.23-1.32)	0.57 (0.32-1.01)	0.56 (0.23-1.34)	0.56 (0.32-1.01)	0.197	0.055
TT+GT	144	87.27	23	95.83	63	91.30	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)		
GG	21	12.73	1	4.17	6	8.70	0.29 (0.03-2.32)	0.65 (0.25-1.69)	0.27 (0.03-2.17)	0.74 (0.28-1.96)	0.222	0.546
rs2227306												
CC	63	38.18	6	25.00	31	44.93	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)		
CT	82	49.70	15	62.50	29	42.03	1.92 (0.70-5.23)	0.72 (0.39-1.31)	1.86 (0.68-5.10)	0.72 (0.39-1.32)	0.228	0.286
TT	20	12.12	3	12.50	9	13.04	1.57 (0.36-6.88)	0.92 (0.37-2.24)	1.64 (0.37-7.24)	0.88 (0.35-2.17)	0.512	0.778
TT+CT	102	61.82	18	75.00	38	55.07	1.85 (0.69-4.92)	0.76 (0.43-1.33)	1.82 (0.68-4.85)	0.75 (0.42-1.33)	0.232	0.327
CC+CT	145	87.88	21	87.50	60	86.96	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)		
TT	20	12.12	3	12.50	9	13.04	1.03 (0.28-3.79)	1.08 (0.46-2.52)	1.10 (0.29-4.08)	1.04 (0.44-2.45)	0.883	0.922
rs2227543												
CC	60	36.36	6	25.00	28	40.58	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)		
CT	83	50.30	14	58.33	31	44.93	1.68 (0.61-4.64)	0.80 (0.43-1.47)	1.62 (0.58-4.49)	0.81 (0.43-1.51)	0.354	0.512
TT	22	13.33	4	16.67	10	14.49	1.82 (0.47-7.05)	0.97 (0.40-2.33)	1.90 (0.48-7.47)	0.92 (0.38-2.24)	0.355	0.865
TT+CT	105	63.64	18	75.00	41	59.42	1.71 (0.65-4.55)	0.83 (0.47-1.48)	1.68 (0.62-4.48)	0.83 (0.46-1.50)	0.302	0.552
CC+CT	143	86.67	20	83.33	59	85.51	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)		
TT	22	13.33	4	16.67	10	14.49	1.30 (0.41-4.16)	1.10 (0.49-2.47)	1.40 (0.43-4.54)	1.03 (0.45-2.35)	0.575	0.930

Furthermore, we carried out stratified analysis of association between rs2069762 polymorphism and acquired AA risk. The analysis results were showed in Table 4. A decreased risk was observed in adults (>16 years old) with GT and GT/GG genotypes.

According to the disease severity, acquired AA could be further subdivided into three groups: vSAA, SAA and NSAA. Since our sample size was small and eight patients lack the information of disease severity, vSAA patients were so little that we combined the vSAA and SAA together to analysis. The distribution of five selected SNPs genotypes were compared

Fig. 1. Transcription factor binding sites showed below the DNA sequence were predicted by TFSearch while it was nucleotide T at rs2069762. Full score was 100, the higher the score the greater the chance.

Fig. 2. No transcription factor binding site was found when it was nucleotide G at rs2069762 predicted by TF-Search.

between each of these two groups and the controls, respectively. As showed in Table 5, no statistical difference was found in our study.

Functional information

Rs2069762 was found located in a transcription factor binding region from SNPinfo. We further predict the potential transcription factor binding sites in rs2069762 by F-SNP. Data shown at this web site was come from the prediction tools of TFSearch. Transcription factor binding sites including CdxA, Abd-B, Skn-1 and BR-C Z were predicted to be exist when nucleotide T located in rs2069762 (Fig. 1). However, no TFBS was found while nucleotide G located in this polymorphic loci (Fig. 2). It indicated that rs2069762 changed the transcriptional regulation.

Moreover, previous researchers had explored whether rs2069762 could affect the transcriptional activity. They conducted experiments of plasmid construction, transfection and luciferase assays. Results showed statistical differences [15]. These information reflected that rs2069762 could ulteriorly influence expression or function of IL-2.

Discussion

According to Neal S.Young's report in 2008, the annual incidence of acquired aplastic anemia in China was about 7.4 per million, approximately 3-fold higher than that in Europe [24]. Though the etiology of acquired AA has some correlations with immune dysregulation, viral infections, drug and chemical exposure, the exact pathogenesis still remains idiopathic

and elusive. Nowadays, scholars mostly agree that acquired AA is an autoimmune disease. About two-thirds of acquired aplastic anemia patients could recover their hematopoietic function after immunosuppressive therapies (IST), serving as an important evidence for the theory that acquired AA is an autoimmune disease [24]. In most cases, the active destruction of hematopoietic cells by effector T lymphocytes is a key factor leading to the occurrence of acquired aplastic anemia. It was found that abnormal activation of Th1 T-cell would make patients' T cells immoderately produce hematopoietic negative regulatory factors, which inhibit the proliferation of HSPC and weaken the hematopoietic regulation mechanism [5].

As an autocrine product from antigen-stimulated T cells, IL-2 induces the production of proinflammatory cytokines like IFN- γ and IL-4, which play a crucial role in proliferation and expansion of both antigen-specific clones of CD4+ and CD8+ T cells [25]. Besides, IL-2 can control and prevent autoimmunity by stimulating T regulatory (CD4+CD25+) cells [26]. IL-8, a member of the chemokine family, can suppress the proliferation of primitive myeloid cells by transducing an inhibitory signal via receptor-ligand-mediated mechanism [27, 28]. Thus, these two cytokines both have subtle effects on the development of acquired aplastic anemia.

SNP is caused by the variation of base sequence at the genome level. The changed genotype may have impacts on DNA transcription or protein structure that could affect receptor binding or protein concentration [29]. Then the biological properties would be affected. In this case, SNP could cause the susceptibility of disease.

As far as we know, this is the first time to investigate the correlation between these five SNPs (rs11575812, rs2069772 and rs2069762 of IL-2, rs2227306 and rs2227543 of IL-8) and the risk of acquired AA in Chinese Han population. Rs2069762, located in a 5' flanking region of IL2, is statistically significant in our study. At the same time, the functional information we found showed that it changed the transcriptional regulation. It was also reported that rs2069762 had an impact on expression of IL-2 [30]. In this case, IL-2 may further negatively affect the T lymphocyte mediated immune response, contributing to the occurrence of acquired aplastic anemia. Moreover, it was also discovered that rs2069762 T to G substitution was associated with the development of other autoimmune diseases, such as multiple sclerosis (MS) in Spanish population [15] and psoriasis in the Northeastern Chinese Han population [31]. Consistently, data in table 4 showed a decreased risk in adults (>16 years old) with GT and GT/GG genotypes. Since our sample size was small, homozygous mutations were too few, possibly making the result biased. In that case, the statistical result of heterozygote might become much more reliable. Therefore, it could be assumed that the rs2069762 T>G mutation might reduce the risk of acquired aplastic anemia in a Chinese population. This conclusion needs to be validated with a larger sample size.

Although according to the results of our study, rs11575812, rs2069772, rs2227306 and rs2227543 might not have association with the occurrence of acquired AA, they have association with other diseases. It was found that mutation in rs11575812 could be associated with SLE risk in a Tunisian population [25]. Henneman et al. reported rs2069772 variant might contribute to the expression of Cow's milk allergy in Dutch children [32]. Polymorphisms of rs2227306 and rs2227543 might confer the development and progression of childhood IgA nephropathy [33]. In addition, unfortunately, no meaningful results were found between the two groups when stratified by the disease severity including NSAA, SAA and vSAA (table 5). However, due to our relatively small sample size, it is hard to draw the conclusion that these five SNPs have no connection with the disease severity; a much larger sample size are needed to consolidate the conclusion.

In conclusion, results in this study suggest that rs2069762 T>G mutation may be associated with a reduced risk for acquired AA in a Chinese population. Although the sample size is relatively small, our findings have provided direction for further research with a much larger sample size. Moreover, based on the results of our study, further epidemiological studies in a larger sample size and functional evaluations could be carried out.

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Disclosure Statement

None declared.

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