Dermatology Practical & Conceptual

Genetic Polymorphisms of miR-146a and miR-155 in Psoriasis and Psoriatic Arthritis: Evidence from a Turkish Case-Control Study

Fadime Mutlu Icduygu[1], Isil Deniz Oguz[2], Egemen Akgun[3], Burak Aksan[2], Sevgi Kulakli[2], Ebru Alp[3]

1 Department of Medical Genetics, Faculty of Medicine, Giresun University, Giresun, Turkey
2 Department of Dermatology, Faculty of Medicine, Giresun University, Giresun, Turkey
3 Department of Medical Biology, Faculty of Medicine, Giresun University, Giresun, Turkey

Key words: Psoriasis, Psoriatic arthritis,MiR-146a, MiR-155, Genetic polymorphism

Citation: Mutlu Icduygu F, Oguz ID, Akgun E, Aksan B, Kulakli S, Alp E. Genetic Polymorphisms of miR-146a and miR-155 in Psoriasis and Psoriatic Arthritis: Evidence from a Turkish Case-Control Study *Dermatol Pract Concept*. 2026;16(1):5977. DOI: https://doi.org/10.5826/dpc.1601a5977

Accepted: September 16, 2025; **Published:** January 2026

Funding: None.

Competing Interests: None.

Authorship: All authors have contributed significantly to this publication.

Corresponding Author: Fadime Mutlu Icduygu, Department of Medical Genetics, Faculty of Medicine, Giresun University, Giresun 28100, Turkey. ORCID ID: 0000-0002-4913-9420. E-mail: fadimemutlu@yahoo.com

ABSTRACT

Introduction: Psoriasis, a widespread inflammatory cutaneous disease, is driven by an interplay of genetic and environmental risk factors. miR-155 and miR-146a have been implicated in the regulation of inflammatory pathways.

Objectives: In the current study, we examined the association between miR-155 rs767649 and miR-146a rs2910164 variants and the predisposition to psoriasis and psoriatic arthritis.

Methods: A total of 544 individuals, including 284 psoriasis cases (68 with psoriatic arthritis) and 260 controls, were enrolled in the present study. Real-time polymerase chain reaction (qPCR) method was used to detect the genotypes of study groups.

Results: The frequencies of the rs2910164 C allele, CC, and GC genotypes were significantly higher in the patient group ($P<0.001$), while the frequencies of the rs767649 A allele and AA genotype were higher in the control group ($P=0.005$ and $P=0.002$, respectively). No statistically significant difference in genotype or allele frequency was observed between patients with and without psoriatic arthritis ($P>0.05$). Rs2910164 CC and GC genotypes were found to be associated with a younger age at disease onset ($P=0.006$), and CC genotype was associated with higher PASI score ($P=0.024$).

Conclusion: The present data suggest an association between the presence of the miR-155 rs767649 and miR-146a rs2910164 variants and susceptibility to psoriasis in the Turkish population. However, although the number of patients with psoriatic arthritis in our study was relatively small, no association was found between these variants and the development of psoriatic arthritis. Furthermore, the rs2910164 polymorphism was found to be associated with both early-onset disease and PASI score.

Introduction

Psoriasis is a widespread chronic inflammatory dermatological condition that manifests in various clinical forms [1,2]. The worldwide prevalence of the disease is estimated to be between 2% and 3% [3]. The most common clinical form is plaque type, also known as psoriasis vulgaris. Other forms include guttate, inverse, pustular, and erythrodermic psoriasis [1-4]. The skin of the patients displays oval salmon-colored lesions covered with white-silver scales, which are raised, itchy, and have well-defined borders. These lesions result from the abnormal proliferation and differentiation of keratinocytes and the activation of immune cells [4,5]. Psoriasis has been associated with a variety of comorbid conditions, including psoriatic arthritis, chronic obstructive pulmonary disease (COPD), metabolic syndrome, cardiovascular disease, depression, diabetes mellitus, gastrointestinal disease, hypertension, and asthma. Therefore, psoriasis has a profound effect on patients' quality of life and causes both physical and psychological difficulties [4-7]. The disease has been reported to have a strong genetic component. Along with environmental factors, it contributes to the development of the disease [1,4,8]. Genome-wide association studies (GWAS) have reported more than 80 loci associated with psoriasis. These loci mostly include genes involved in adaptive and innate immune system processes (antigen presentation, skin barrier protection, the nuclear factor kappa B (NF-kB), IL23/Th17 axis and type I interferon signaling pathways) such as ERAP1, HLA-C, LCE3, KLF4, IL23A, IL23B, TYK2, IRF4, IL12B, IFIH1, EXOC2, RNF114, TNIP1, TRAF3IP2, and CARD14 [1,4,9,10]. On the other hand, studies have revealed that epigenetic regulators such as microRNAs (miRNAs) also make an important contribution to psoriasis susceptibility [5,11].

Psoriatic arthritis is a chronic inflammatory arthropathy that occurs in approximately 30% of psoriasis patients [12]. As in psoriasis, genetic, environmental, and epigenetic factors have been identified as contributing to the etiopathogenesis of psoriatic arthritis. Although there are many common gene variants linked to the risk of developing psoriatic arthritis and psoriasis, the presence of gene variants such as IL-4 and KIF3A variants, which are only related to the risk of developing psoriatic arthritis, suggests that there are distinct molecular mechanisms underlying the development and progression of psoriatic arthritis [13].

miRNAs are short non-coding RNAs with a length of 20 to 24 nucleotides. These RNA molecules are post-transcriptional regulators of gene expression. They bind the 3' untranslated region (UTR) region of target mRNA molecules, which enables mRNA degradation or inhibits translation [11,14]. miRNAs are involved in a wide range of physiological events, including cell cycle regulation, differentiation, metabolic pathways, apoptosis, and immune system processes [11,15]. Polymorphisms in the genes encoding miRNAs lead to changes in miRNA expression or structure. These changes affect miRNA function and play a role in the emergence of various diseases [15,16].

miR-146a, encoded in the 5q34 region, is known to be involved in immune response [15,16]. Previous studies have demonstrated that miR-146a negatively regulates inflammation. The binding of miR-146a to TNF receptor-associated factor 6 (TRAF6) and interleukin 1 receptor-associated kinase 1 (IRAK1), genes in the NF-κB pathway, results in a decrease in their expressions and the suppression of the release of proinflammatory cytokines in myeloid and T cells [17-19]. The rs2910164 polymorphism has been demonstrated to be involved in the miR-146a precursor and to alter the expression level of mature miR-146a [16]. This variant has been associated with various cancer types and autoimmune diseases in the literature [17,20-22]. Nevertheless, the number of studies investigating its association with psoriasis and psoriatic arthritis is limited, and the results obtained from different populations appear contradictory [13,16,23].

miR-155, encoded in the 21q21.3 region, contributes to the regulation of innate and adaptive immune responses as well as to cell cycle, cell proliferation, and apoptosis [18,24,25]. Suppressor of cytokine signaling 1 (SOCS1), one of the target genes of miR-155, negatively regulates the JAK/STAT signaling pathway and is an inhibitor of IL17. Consequently, elevated miR-155 expression has been linked to various autoimmune disorders [18]. Its expression has been observed to be elevated in diseased tissues and blood mononuclear cells of psoriasis patients in comparison with those of control individuals [24,26]. The rs767649 polymorphism of the miR-155 gene has been demonstrated to reduce miR-155 expression [27].

Objectives

A search of the literature revealed that no study has yet been undertaken to investigate whether there is a relationship between miR-155 polymorphisms and susceptibility to psoriasis and psoriatic arthritis. Furthermore, the association between mir146a and mir155 variants and psoriasis and psoriatic arthritis has not yet been determined in the Turkish population. Consequently, the current study purposed to investigate the relationship between psoriasis/psoriatic arthritis and miR-146a rs2910164 and miR-155 rs767649 polymorphisms in the Turkish population.

Methods

Participants

The Declaration of Helsinki was followed during the research, and the current study was approved by Giresun University's Faculty of Medicine Clinical Trials Ethics Committee (Approval Number: 18.03.2021-07). Each subject signed an informed consent form prior to enrollment. A total of 544 participants were enrolled in the study, comprising 284 psoriasis patients (68 with psoriatic arthritis) diagnosed by dermatologists at Giresun University Faculty of Medicine Dermatology outpatient clinic and 260 controls without psoriasis. Patients were selected from individuals who did not have autoimmune or systemic diseases other than psoriasis. The control group was selected from individuals without any autoimmune or systemic disease and without a family history of psoriasis. The clinical and demographic characteristics of the cases, including the distribution of lesions, psoriasis subtypes, presence of psoriatic arthritis, and psoriasis area and severity index (PASI), were recorded.

DNA Extraction and Genotyping

DNA extraction was conducted on blood samples in EDTA tubes obtained from the study group utilizing the High Pure PCR Template Preparation Kit (Roche Diagnostics, Mannheim, Germany) following the manufacturer's recommendations. Genotypes were determined by real-time polymerase chain reaction (qPCR) on the LightCycler 480 with the use of the FastStart DNA Master HybProbe (Roche Diagnostics, GmBH, Mannheim, Germany) and the appropriate primer probe set. The following primers were used: F;5'-CGATGTGTATCCTCAGCTTTGA-3' and R;5'- TGAGACTCTGCCTTCTGTCT-3' for rs2910164, F;5'- TTCGGAATTCATCATGCCTGTA-3' and R; 5'-GCTGGCATACTATTCTACCCATAA-3' for rs767649. PCR conditions were: 10 min at 95° C for denaturation, continued for 60 cycles of (5 s at 95° C, 10 s at 60° C , 10s at 50° C , 10 s at 72° C) for amplification, and 20 s at 95° C, 20 s at 32° C for melting curve analysis. As positive and negative controls, heterozygous DNA samples / distilled water were used. The genotyping results were confirmed by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) method in twenty randomly selected samples from the cases and controls.

Statistical Analysis

Statistical analyses were accomplished by the IBM SPSS Statistics® version 25 (IBM Corp, Armonk, NY, USA). The G-Power 3.1 program was employed for the purpose of power analysis. Quantitative data are represented as mean ± standard deviation, while qualitative data are represented as numbers (percentage). The chi-square ($\chi 2$) test was employed to ascertain whether the genotype frequencies were in agreement with the Hardy-Weinberg equilibrium (HWE). The Mann-Whitney test was employed to examine the statistical significance of differences in quantitative variables between groups. To analyze allele and genotype frequencies between the groups, $\chi 2$ test was utilized. Odds ratios (OR) and confidence intervals (CI) were calculated according to the reference genotype to determine the strength of association. The relationship between genotypes and clinical features was analyzed using $\chi 2$ tests for qualitative variables and one-way ANOVA test with Tukey's post hoc test for quantitative variables. P-values were interpreted as statistically significant if they were below 0.05. Logistic regression analysis was employed to analyze the independent effect of polymorphisms from other risk factors. Finally, to reduce the likelihood of false positive results in the logistic regression analysis, the confidence interval was increased to 99%, and p-values less than 0.01 were considered significant.

Results

The initial power analysis revealed that a final sample size of 317 would be necessary to achieve a 0.05 type I error rate, an effect size of 0.20, and 90% statistical power. Genotyping was performed for rs2910164 and rs767649 polymorphisms in 282 patients and 232 control samples, and in 271 patients and 250 controls, respectively. In total, 544 cases were included in the study. The genotype frequencies of the rs2910164 polymorphism were in agreement with the Hardy-Weinberg equilibrium (HWE) in cases and controls. In contrast, rs767649 genotype frequencies exhibited deviations from HWE in both groups (Table 2). It is unlikely that these deviations were due to genotyping errors, as they were confirmed by using a different method involving twenty randomly selected patients. Table 1 demonstrates the clinical and demographic characteristics of the patient and control groups. The patient and control groups differed significantly in terms of age and sex ($P<0.001$ and $P=0.005$, respectively).

Table 1. Demographic and clinical characteristics of study groups.

Variable	Case (N=284)	Control (N=260)	*p*-value
Age (years), (mean ± SD)	46 ± 14.8	37 ± 16.4	**<0.001**
Sex			
Female N (%)	146 (51.4)	165 (63.2)	**0.005**
Male N (%)	138 (48.6)	95 (36.4)	
Age of onset (years), (mean ± SD)	30 ± 15.6	-	
Duration of disease (years), (mean ± SD)	16 ± 12.5	-	
PASI (mean ± SD)	7.9 ± 8.2	-	
PASI			
Positive family history n (%)	126 (44.4)	-	
Distribution			
Scalp	185 (65.1)	-	
Nail	105 (37)	-	
Genital	50 (17.6)	-	
Joint	47 (16.5)	-	
Psoriatic arthritis	68 (23.9)	-	
Type of psoriasis N (%)			
Plaque	226 (79.6)	-	
Guttate	1 (0.4)	-	
Inverse	6 (2.1)	-	
Erythrodermic	4 (1.4)	-	
Palmoplantar	10 (3.5)	-	
Localized pustular	7 (2.5)	-	
Generalized pustular	1 (0.4)	-	
Mix	29 (10.2)	-	

PASI, Psoriasis Area and Severity Index, The Mann-Whitney test and the chi-square test were used to compare age and sex, respectively, between the groups.

Genotype and Allele Frequencies between Psoriasis Patients and Controls

Table 2 presents a summary of the genotype and allele distribution between psoriasis patients and the control group. The results indicate that the rs2910164 C allele, CC, and GC genotype frequencies were significantly higher in the patient group compared to the control group ($P<0.001$). In addition, while similar significance was observed in the dominant and recessive models ($P<0.001$), no significant association was observed in the overdominant model ($P=0.114$).

For the Rs767649 polymorphism, the frequencies of the A allele ($P=0.005$) and the AA genotype ($P=0.011$) were significantly higher in the control group compared to the patient group. A borderline significant association was identified in the dominant model ($P=0.049$), while a significant difference was observed in the recessive model ($P=0.019$) (Table 2).

Binary logistic regression analysis was then performed including possible co-founders (age and sex). The data obtained after logistic regression analysis revealed that the GC genotype increased the risk of disease 3.83-fold and the CC genotype 5.22-fold compared to the rs2910164 GG genotype ($P<0.001$). While significance remained in the dominant and recessive models ($P<0.001$), no significant association was observed in the overdominant model ($P=0.145$). In addition, the AA genotype of the rs767649 polymorphism was associated with a 2.2-fold reduction in disease risk compared to the TT genotype ($P=0.002$). Borderline significance was observed in the dominant and recessive models for rs767649 polymorphism ($P=0.012$ and $P=0.010$, respectively) (Table 2).

Distribution of Genotype and Allele Frequencies in Patients With and Without Psoriatic Arthritis

There was no significant difference in genotype and allele frequencies between patients with and without psoriatic arthritis ($P>0.05$). When each of these groups was compared separately with the control group, the frequencies of the C allele ($P<0.001$ for both groups), GC genotype ($P=0.002$ for the group with psoriatic arthritis,

Table 2. Distribution of genotype and allele frequencies between psoriasis patients and controls.

Genotypes and alleles	Cases N (%)	Controls N (%)	OR (95%CI)	*p*-value	AOR (99% CI)	*Adjusted p-value*
Rs2910164						
GG	31 (11)	82 (32.8)	Ref		Ref	
GC	132 (46.8)	100 (40)	3.49 (2.14-5.69)	**<0.001**	3.83 (1.91-7.71)	**<0.001**
CC	119 (42.2)	68 (27.2)	4.63 (2.78-7.70)	**<0.001**	5.22 (2.51-10.86)	**<0.001**
GC+CC vs GG (Dominant Model)	251 (89)	168 (67.2)	3.95 (2.50-6.24)	**<0.001**	4.3 (2.24-8.26)	**<0.001**
GG+GC vs CC (Recessive Model)	163 (57.8)	182 (72.8)	0.51 (0.36-0.74)	**<0.001**	0.49 (0.29-0.82)	**<0.001**
GG+CC vs GC (Overdominant Model)	150 (53.2)	150 (60)	0.76 (0.54-1.07)	0.114	0.76 (0.47-1.23)	0.145
G	194 (34.4)	264 (52.8)	Ref			
C	370 (65.6)	236 (47.2)	2.13 (1.67-2.73)	**<0.001**		
	HWE: 0.711	HWE: 0.048				
Rs767649						
TT	116 (42.8)	86 (34.4)	Ref			
TA	97 (35.8)	88 (35.2)	0.82 (0.55-1.22)	0.324	0.74 (0.41-1.32)	0.182
AA	58 (21.4)	76 (30.4)	0.57 (0.36-0.88)	**0.011**	0.46 (0.24-0.88)	**0.002**
TA+AA vs TT (Dominant Model)	155 (57.2)	164 (65.6)	0.70 (0.49-0.99)	**0.049**	0.60 (0.36-1.02)	**0.012**
TT+TA vs AA (Recessive Model)	213 (78.6)	174 (69.6)	1.60 (1.08-2.38)	**0.019**	1.76 (1-3.09)	**0.010**
TT+AA vs TA (Overdominant Model)	174 (64.2)	162 (64.8)	0.97 (0.68-1.40)	0.888	0.99 (0.60-1.65)	0.989
T	329 (60.7)	260 (52)	Ref			
A	213 (39.3)	240 (48)	0.70 (0.55-0,90)	**0.005**		
	HWE: 0.012	HWE: 0.003				

OR, odds ratio; AOR, adjusted odds ratio, 95% CI, 95% confidence intervals. Chi-square test was used to compare genotype and allele frequencies between groups. The AOR with their 99 % CIs was estimated by binary logistic regression models after controlling for age and sex.

P<0.001 for the group without psoriatic arthritis), and CC genotype (*P*<0.001 for both groups) were found to be higher compared to the control group (Tables 3 and 4). On the other hand, no significant difference was observed between the group with psoriatic arthritis and the control group in terms of rs767649 polymorphism (*P*>0.05) (Table 3). However, when psoriasis patients without psoriatic arthritis were compared with the control group, AA genotype (*P*=0.020) and A allele frequency (*P*=0.008) were significantly higher in the control group, while there was borderline significance in the dominant (*P*=0.049) and recessive model (*P*=0.042) (Table 4). Similar results were obtained in logistic regression analysis including age and sex (Tables 3 and 4).

Table 3. Distribution of genotype and allele frequencies between patients with psoriatic arthritis and controls.

Genotypes and alleles	Patients with psoriatic arthritis (%)	Controls N (%)	OR (95%CI)	*p*-value	AOR (99% CI)	*Adjusted p-value*
Rs2910164						
GG	7 (10.3)	82 (32.8)	Ref			
GC	32 (47.1)	100 (40)	3.75 (1.57-8.93)	**0.002**	4.67 (1.34-16.42)	**0.002**
CC	29 (42.6)	68 (27.2)	4.99 (2.06-12.11)	**<0.001**	6.53 (1.82-23.40)	**<0.001**
GC+CC vs GG (Dominant Model)	61 (89.7)	168 (67.2)	4.25 (1.86-9.71)	**<0.001**	5.41 (1.64-17.84)	**<0.001**
GG+GC vs CC (Recessive Model)	39 (57.4)	182 (72.8)	0.50 (0.29-0.88)	**0.014**	0.46 (0.21-0.99)	**0.009**
GG+CC vs GC (Overdominant Model)	36 (52.9)	150 (60)	0.75 (0.44-1.29)	0.295	0.76 (0.36-1.60)	0.348
G	46 (33.8)	264 (52.8)	Ref			
C	90 (66.2)	236 (47.2)	2.19 (1.47-3.25)	**<0.001**		
Rs767649						
TT	27 (40.9)	86 (34.4)	Ref			
TA	26 (39.4)	88 (35.2)	0.94 (0.51-1.74)	0.847	0.86 (0.36-2.07)	0.653
AA	13 (19.7)	76 (30.4)	0.55 (0.26-1.13)	0.100	0.52 (0.19-1.44)	0.098
TA+AA vs TT (Dominant Model)	39 (59.1)	164 (65.6)	0.76 (0.44-1.32)	0.326	0.69 (0.31-1.51)	0.218
TT+TA vs AA (Recessive Model)	53 (80.3)	174 (69.6)	1.78 (0.92-3.46)	0.086	1.68 (0.68-4.16)	0.139
TT+AA vs TA (Overdominant Model)	40 (60.6)	162 (64.8)	0.84 (0.48-1.46)	0.528	0.87 (0.41-1.87)	0.641
T	80 (60.6)	270 (52.9)	Ref			
A	52 (39.4)	240 (47.1)	0.73 (0.50-1.08)	0.115		

OR, odds ratio; AOR, adjusted odds ratio, 95% CI, 95% confidence intervals. Chi-squared test was used to compare genotype and allele frequencies between groups. The AOR with their 99 % CIs was estimated by binary logistic regression models after controlling for age and sex.

Relationship between Genotypes and Clinical Parameters

Table 5 depicts the data on the association between clinical parameters and genotypes. Accordingly, a significant association was found between age at disease onset and both polymorphisms (P=0.006 for rs2910164 and P=0.045 for rs767649). Post hoc analyses showed that the GC (P=0.004) and CC (P=0.047) genotypes were associated with an earlier age at disease onset compared to the rs2910164 GG genotype. On the other hand, post hoc analyses for rs767649 showed that there was no significant association between age at disease onset and genotypes.

The genotype distribution of those with a PASI ≤10 and those with a PASI >10 showed that rs2910164 polymorphism

Table 4. Distribution of genotype and allele frequencies between patients without psoriatic arthritis and controls.

Genotypes and alleles	Patients without psoriatic arthritis (%)	Controls N (%)	OR (95%CI)	*p*-value	AOR (99% CI)	*Adjusted p-value*
Rs2910164						
GG	24 (11.2)	82 (32.8)	Ref		Ref	
GC	100 (46.7)	100 (40)	3.42 (2-5.82)	**<0.001**	3.44 (1.63-7.27)	**<0.001**
CC	90 (42.1)	68 (27.2)	4.52 (2.6-7.86)	**<0.001**	4.65 (2.12- 10.18)	**<0.001**
GC+CC vs GG (Dominant Model)	190 (88.8)	168 (67.2)	3.86 (2.34-6.37)	**<0.001**	3.86 (1.91-7.76)	**<0.001**
GG+GC vs CC (Recessive Model)	124 (57.9)	182 (72.8)	0.52 (0.35-0.76)	**0.001**	0.51 (0.29-0.89)	**0.002**
GG+CC vs GC (Overdominant Model)	114 (53.3)	150 (60)	0.76 (0.53-1.10)	0.145	0.75 (0.45-1.27)	0.162
G	148 (34.6)	264 (52.8)	Ref			
C	280 (65.4)	236 (47.2)	2.11 (1.62-2.76)	**<0.001**		
Rs767649						
TT	89 (43.4)	86 (34.4)	Ref			
TA	71 (34.6)	88 (35.2)	0.78 (0.51-1.20)	0.257	0.71 (0.38-1.34)	0.164
AA	45 (22)	76 (30.4)	0.57 (0.36-0.92)	**0.020**	0.46 (0.23-0.92)	**0.004**
TA+AA vs TT (Dominant Model)	116 (56.6)	164 (65.6)	0.68 (0.47-0.99)	**0.049**	0.60 (0.34-1.04)	**0.017**
TT+TA vs AA (Recessive Model)	160 (78)	174 (69.6)	1.55 (1.01-2.38)	**0.042**	1.76 (0.96-3.23)	**0.016**
TT+AA vs TA (Overdominant Model)	134 (65.4)	162 (64.8)	1.03 (0.70-1.51)	0.900	1.03 (0.60-1.78)	0.874
T	249 (60.7)	260 (52)	Ref			
A	161 (39.3)	240 (48)	0.70 (0.54-0.91)	**0.008**		

OR, odds ratio; AOR, adjusted odds ratio, 95% CI, 95% confidence intervals. Chi-squared test was used to compare genotype and allele frequencies between groups. The AOR with their 99 % CIs was estimated by binary logistic regression models after controlling for age and sex.

was associated with PASI score (*P*=0.024) (Table 5). Post hoc analysis revealed that the frequency of individuals with a PASI >10 was significantly higher in those carrying the CC genotype compared to the GC genotype (*P*=0.010). No significant association was found between polymorphisms and other clinical parameters. When only patients with psoriatic arthritis were evaluated, no significant association was found between clinical parameters and genotypes (*P*>0.05). In contrast, when only psoriasis patients without psoriatic arthritis were evaluated, rs2910164 polymorphism was associated with age at disease onset (*P*=0.025) and PASI score (*P*=0.013), similar to the entire patient group.

Discussion

miR-146a and miR-155 have been proposed to regulate keratinocyte proliferation and differentiation as well as the immune response and inflammatory processes. Furthermore, studies have shown that their expression levels vary in psoriasis patients [11,28-30]. In this study, we assessed the association between miR-146a rs2910164 and miR-155 rs767649 variants with the development of psoriasis/psoriatic arthritis and clinical features of the disease in the Turkish population. Our data demonstrated that the GC and CC genotypes and the C allele of the rs2910164 polymorphism were strongly

Table 5. Genotype frequencies of rs2910164 and rs767649 in psoriasis patients grouped according to clinical characteristics.

Variations	Rs2910164				Rs767649			
Genotypes	GG	GC	CC	*p*-value	TT	TA	AA	p-value
Sex								
Female N (%)	18 (12.3)	70 (47.9)	58 (39.7)	0.602	59 (41.3)	57 (39.9)	27 (18.9)	0.291
Male N (%)	13 (9.6)	62 (45.6)	61 (44.9)		57 (44.5)	40 (31.3)	31 (24.2)	
Age at onset (mean ± SD)	37.7±16.3	27.9±14.5	30.3±16.2	**0.006**	27.3±13.6	31.3±16.6	33±16.6	**0.045**
PASI mean	7.5±8.4	7±7.4	9.2±8.9	0.114	8.8±9.4	7±7.4	7.9±7.5	0.288
PASI								
≤10	24 (12.1)	101(50.8)	74 (37.2)	**0.024**	79 (41.4)	70 (36.6)	42 (22)	0.709
>10	7 (8.5)	30 (36.6)	45 (54.9)		37 (46.8)	26 (32.9)	16 (20.3)	
Family history								
No	19 (12.1)	73 (46.5)	65 (41.4)	0.796	57 (37.7)	58 (38.4)	36 (23.8)	0.162
Yes	12 (9.6)	59 (47.2)	54 (43.2)		59 (49.2)	39 (32.5)	22 (18.3)	
Psoriatic arthritis								
No	24 (11.2)	100(46.7)	90 (42.1)	0.978	89 (43.4)	71 (34.6)	45 (22)	0.776
Yes	7 (10.3)	32 (47.1)	29 (42.6)		27 (40.9)	26 (39.4)	13 (19.7)	

PASI, Psoriasis Area and Severity Index, One-way ANOVA test (for continuous variables) or chi-square test (for categorical variables) was used to compare clinical characteristics between groups.

associated with susceptibility to the disease in our population (Table 2). On the other hand, the AA genotype and the A allele of the rs767649 polymorphism were associated with a reduced risk of developing psoriasis (Table 2).

A number of studies have shown that changes in miR-146a expression and polymorphisms of the gene encoding miR-146a are associated with many diseases, especially various types of cancer and autoimmune diseases [13,17,20,22,31]. A research study conducted in the Han Chinese population investigated the association between psoriasis and the rs2910164 polymorphism. This study found that the G allele was associated with an elevated risk of psoriasis [16]. Similarly, the G allele was discovered to be associated with an enhanced susceptibility to psoriasis and psoriatic arthritis in Italian patients [13]. In a further study conducted on Caucasian individuals in Sweden, it was reported that the CC genotype was found to be protective against psoriasis in parallel with these studies [32]. In contrast, Maharaj et al. reported that the C allele was associated with the risk of psoriatic arthritis within the Indian population [15]. A meta-analysis of the aforementioned studies indicated that the CC genotype was related with a low risk of developing psoriasis [23]. The data obtained from the present study were consistent with the data of Maharaj et al.[15] but different from the results of other studies. We think that the most important reason for the discordance between the results is due to ethnicity differences. Indeed, NCBI data reveal that allele frequencies for this polymorphism are highly variable between ethnic groups. For example, in East Asian populations including China, allele C is a major allele (allele frequency (AF): 0.62), while in European populations allele C is a minor allele (AF: 0.23). In our study, the minor allele was C allele, and its frequency in the control group was 0.47. According to NCBI data, it seems to be closest to the frequency in the African population (C allele frequency: 0.37-0.44) [33]. The study by Maharaj et al., with whose results ours are compatible, was also conducted on individuals of South African origin [15]. Since allele frequencies can differ markedly among populations, the generalizability of our findings may be limited. Therefore, replication of these associations in other ethnic groups will be important to clarify potential population-specific genetic effects.

The rs2910164 C allele causes a mismatch in the hairpin of the pre-miRNA, which alters the minimum free energy of the molecule (–43.1 kcal/mol for the G allele, –40.3 kcal/mol for the C allele) and makes the secondary structure less stable and/or efficient. [34,35]. Jazdzewski et al. observed a greater decrease in IRAK and TRAF-6 luciferase levels in cells treated with plasmids carrying the miR-146a G allele compared to those carrying the miR-146a C allele [34]. Therefore, carriers of the rs2910164 C allele may have decreased inhibition of IRAK and TRAF6 proteins, which are key players in the proinflammatory signaling cascade. This may lead to an increased inflammatory response and

predisposition to psoriasis in carriers of the rs2910164 C allele, which supports our findings.

Some studies have reported an increase in miR-155 expression in various samples obtained from psoriasis patients, including skin tissue, peripheral blood mononuclear cells, and serum [28,29]. However, no study investigating the relationship between susceptibility to psoriasis and miR-155 polymorphisms was found in the literature. Nevertheless, the miR-155 rs767649 polymorphism has been investigated in relation to autoimmune diseases such as rheumatoid arthritis, Behçet's disease, multiple sclerosis, systemic lupus erythematosus (SLE), and various cancers [36-45]. The TT genotype and T allele in two studies on SLE [36,37], the T allele in multiple sclerosis [38], and the TT genotype in Behçet's disease [39] and rheumatoid arthritis [41] were found to be associated with an increased risk. Similarly, the AA genotype and A allele were reported to be protective in another study conducted on rheumatoid arthritis patients [40]. In our study, the AA genotype and A allele were associated with a lower risk of psoriasis development. Our results appear to be consistent with those of other studies [36-44] . There are some studies in the literature showing that rs767649 polymorphism decreases miR-155 expression [41,44]. Consequently, it is possible to conclude that the A allele/AA genotype is associated with decreased miR-155 expression. Although further functional studies are required to confirm this association, it is plausible that decreased miR-155 expression may be associated with increased SOCS1 expression (a negative regulator of the JAK/STAT pathway and an inhibitor of IL17), which may subsequently result in a reduced risk of psoriasis through reduced cytokine release and inflammation.

Analyzing the relationship between clinical findings and these polymorphisms, it was observed that the allele and genotype frequencies of both polymorphisms were not different between the patient groups with and without psoriatic arthritis ($P>0.05$). However, the C allele, GC and CC genotypes of rs2910164 polymorphism were found to be higher in the patient groups with and without psoriatic arthritis compared to the control group (Tables 3 4). When the same comparison was made for the rs767649 polymorphism, the A allele and the AA genotype were found to be higher in the control group compared to psoriasis patients without psoriatic arthritis (Table 4). Besides the common mechanisms involved in developing psoriasis and psoriatic arthritis, mechanisms associated only with developing psoriatic arthritis have been reported [46]. Our results suggest that these two polymorphisms may play a role in the development of these diseases through the above-mentioned common mechanisms leading to increased inflammation, but they do not contribute additionally to the development of psoriatic arthritis in patients with psoriasis. However, we should note that the number of patients with psoriatic arthritis in our study was relatively small, and this limitation should be taken into account when evaluating the results regarding the relationship between polymorphisms and the development of psoriatic arthritis. Furthermore, the rs2910164 GC and CC genotypes and the rs767649 TT genotype were related with an earlier age at disease onset, while the rs2910164 CC genotype was associated with a higher PASI score (Table 5). Limitations of our study include the small number of patients with psoriatic arthritis and the lack of functional studies on the potential mechanisms of action of these polymorphisms.

Conclusion

In summary, the present study revealed that miR-146a rs2910164 and miR-155 rs767649 polymorphisms predispose to psoriasis in our study group. However, these variants were not associated with the development of psoriatic arthritis in psoriasis patients. Nevertheless, the rs2910164 polymorphism was associated with earlier age at onset and higher PASI score. Future studies in larger and ethnically diverse populations are warranted to validate these findings and to clarify their potential implications for risk stratification and personalized management in psoriasis.

Acknowledgments: The DeepL language platform was used to correct translation and grammatical errors.

References

1. Griffiths CEM, Armstrong AW, Gudjonsson JE, Barker JNWN. Psoriasis. *Lancet (London, England)*. 2021;397(10281):1301-1315. DOI:10.1016/S0140-6736(20)32549-6 PMID: 33812489.
2. Yang SF, Lin MH, Chou PC, et al. Genetics of Generalized Pustular Psoriasis: Current Understanding and Implications for Future Therapeutics. *Genes (Basel)*. 2023;14(6):1297. DOI:10.3390/GENES14061297 PMID: 37372477.
3. Guo J, Zhang H, Lin W, Lu L, Su J, Chen X. Signaling pathways and targeted therapies for psoriasis. *Signal Transduct Target Ther*. 2023;8(1):437. DOI:10.1038/S41392-023-01655-6 PMID: 38008779
4. Raharja A, Mahil SK, Barker JN. Psoriasis: a brief overview. *Clin Med (Northfield Il)*. 2021;21(3):170. DOI:10.7861/CLINMED.2021-0257 PMID: 34001566
5. Mateu-Arrom L, Puig L. Genetic and Epigenetic Mechanisms of Psoriasis. *Genes (Basel)*. 2023;14(8):1619. DOI:10.3390/GENES14081619 PMID: 37628670
6. Bu J, Ding R, Zhou L, Chen X, Shen E. Epidemiology of Psoriasis and Comorbid Diseases: A Narrative Review. *Front Immunol*.2022;13:880201.DOI:10.3389/FIMMU.2022.880201 PMID: 35757712
7. Yamazaki F. Psoriasis: Comorbidities. *J Dermatol*. 2021;48(6):732-740. DOI:10.1111/1346-8138.15840 PMID: 33763899
8. Kiełbowski K, Bakinowska E, Ostrowski P, et al. The Role of Adipokines in the Pathogenesis of Psoriasis. *Int J Mol Sci*. 2023;24(7):6390. DOI:10.3390/IJMS24076390 PMID: 37047363
9. Dand N, Mahil SK, Capon F, Smith CH, Simpson MA, Barker JN. Psoriasis and Genetics. *Acta Derm Venereol*. 2020;100(3):54-64. DOI:10.2340/00015555-3384 PMID: 31971603

10. Ogawa K, Okada Y. The current landscape of psoriasis genetics in 2020. *J Dermatol Sci*. 2020;99(1):2-8. DOI:10.1016/J.JDERMSCI.2020.05.008 PMID: 32536600
11. Jiang X, Shi R, Ma R, et al. The role of microRNA in psoriasis: A review. *Exp Dermatol*. 2023;32(10):1598-1612. DOI:10.1111/exd.14871 PMID: 37382420
12. Shao LN, Wang N, Zhou SH, Wang Z. Associations between human leukocyte antigen C locus polymorphism and psoriatic arthritis in populations of European and Middle Eastern descent: a meta-analysis. *Ann Saudi Med*. 2020;40(4):338. DOI:10.5144/0256-4947.2020.338 PMID: 32757989
13. Caputo V, Strafella C, Termine A, et al. RNAseq-Based Prioritization Revealed COL6A5, COL8A1, COL10A1 and MIR146A as Common and Differential Susceptibility Biomarkers for Psoriasis and Psoriatic Arthritis: Confirmation from Genotyping Analysis of 1417 Italian Subjects. *Int J Mol Sci*. 2020;21(8):2740. DOI:10.3390/IJMS21082740 PMID: 32326527
14. Ghosh D, Ganguly T, Chatterjee R. Emerging roles of noncoding RNAs in psoriasis pathogenesis. *Funct Integr Genomics*. 2023;23(2). DOI:10.1007/S10142-023-01057-5 PMID: 37072609
15. Maharaj AB, Naidoo P, Ghazi T, et al. MiR-146a G/C rs2910164 variation in South African Indian and Caucasian patients with psoriatic arthritis. *BMC Med Genet*. 2018;19(1):48. DOI:10.1186/S12881-018-0565-1 PMID: 29587639
16. Zhang W, Yi X, Guo S, et al. A single-nucleotide polymorphism of miR-146a and psoriasis: an association and functional study. *J Cell Mol Med*. 2014;18(11):2225-2234. DOI:10.1111/JCMM.12359 PMID: 25209759
17. Park R, Lee WJ, Ji JD. Association between the three functional miR-146a single-nucleotide polymorphisms, rs2910164, rs57095329, and rs2431697, and autoimmune disease susceptibility: A meta-analysis. *Autoimmunity*. 2016;49(7):451-458. DOI:10.3109/08916934.2016.1171854 PMID: 27098222.
18. Nani P, Ladopoulou M, Papaioannou EH, et al. Pharmacogenetic Analysis of the MIR146A rs2910164 and MIR155 rs767649 Polymorphisms and Response to Anti-TNF Treatment in Patients with Crohn's Disease and Psoriasis. *Genes (Basel)*. 2023;14(2):445. DOI:10.3390/GENES14020445/S1 PMID: 36833372
19. Chatzikyriakidou A, Voulgari P V., Georgiou I, Drosos AA. The role of microRNA-146a (miR-146a) and its target IL-1R-associated kinase (IRAK1) in psoriatic arthritis susceptibility. *Scand J Immunol*. 2010;71(5):382-385. DOI:10.1111/J.1365-3083.2010.02381.X PMID: 20500689.
20. Hao X, Xia L, Qu R, Yang X, Jiang M, Zhou B. Association between miR-146a rs2910164 polymorphism and specific cancer susceptibility: an updated meta-analysis. *Fam Cancer*. 2018;17(3):459-468. DOI:10.1007/S10689-017-0056-0 PMID: 29127520.
21. Wang D, Wang Y, Lin Z, Cai L. Association between miRNA-146a polymorphism and lung cancer susceptibility: A meta-analysis involving 6506 cases and 6576 controls. *Gene*. 2020;757:144940. DOI:10.1016/J.GENE.2020.144940 PMID: 32640303.
22. Wang BR, Chang WS, Liao CH, et al. Impacts of Mir146a Genotypes on Bladder Cancer Risk in Taiwan. *Biomedicines*. 2023;11(5):1396. DOI:10.3390/BIOMEDICINES11051396 PMID: 37239070.
23. Gong HB, Zhang SL, Wu XJ, Pu XM, Kang XJ, Marzano AV. Association of rs2910164 polymorphism in MiR-146a gene with psoriasis susceptibility: A meta-analysis. *Medicine (Baltimore)*. 2019;98(6):e14401. DOI:10.1097/MD.0000000000014401 PMID: 30732186.
24. Ghafouri-Fard S, Eghtedarian R, Taheri M, Rakhshan A. The eminent roles of ncRNAs in the pathogenesis of psoriasis. *Non-coding RNA Res*. 2020;5(3):99-108. DOI:10.1016/J.NCRNA.2020.06.002 PMID: 32695942.
25. Soonthornchai W, Tangtanatakul P, Meephansan J, et al. Down-regulation of miR-155 after treatment with narrow-band UVB and methotrexate associates with apoptosis of keratinocytes in psoriasis. *Asian Pacific J allergy Immunol*. 2021;39(3):206-213. DOI:10.12932/AP-031218-0451 PMID: 30904000.
26. Guo W, Xu F, Zhuang Z, Liu Z, Xie J, Bai L. Ebosin Ameliorates Psoriasis-Like Inflammation of Mice via miR-155 Targeting tnfaip3 on IL-17 Pathway. *Front Immunol*. 2021;12:662362. DOI:10.3389/FIMMU.2021.662362/FULL PMID: 33981308.
27. Iranparast S, Tahmasebi-Birgani M, Motamedfar A, Amari A, Ghafourian M. miR-155 rs767649 T>A gene polymorphism is associated with downregulation of miR-155 expression, suppressor of cytokine signaling-1 overexpression, and low probability of metastatic tumor at the time of breast cancer diagnosis. *J Res Med Sci*. 2023;28(1):32. DOI:10.4103/JRMS.JRMS_960_21 PMID: 37213455.
28. Beer L, Kalinina P, Köcher M, et al. miR-155 Contributes to Normal Keratinocyte Differentiation and Is Upregulated in the Epidermis of Psoriatic Skin Lesions. *Int J Mol Sci*. 2020;21(23):1-16. DOI:10.3390/IJMS21239288 PMID: 33291448.
29. Gu D, Cheng M, Feng J. Expression of miR-155 and miR-146a in Skin Tissue, Peripheral Blood Mononuclear Cells and Serum of Patients with Psoriasis and Its Clinical Significance. *Adv Biosci Biotechnol*. 2022;13:207-215. DOI:10.4236/abb.2022.134011
30. Leal B, Carvalho C, Ferreira AM, et al. Serum Levels of miR-146a in Patients with Psoriasis. *Mol Diagn Ther*. 2021;25(4):475-485. DOI:10.1007/S40291-021-00531-9 PMID: 33937970.
31. Avgeros C, Patsatsi A, Dimitriadis D, et al. Dysregulation of Plasma miR-146a and miR-155 Expression Profile in Mycosis Fungoides Is Associated with rs2910164 and rs767649 Polymorphisms. *Int J Mol Sci*. 2022;24(1):271. DOI:10.3390/IJMS24010271 PMID: 36613718.
32. Srivastava A, Nikamo P, Lohcharoenkal W, et al.MicroRNA-146a suppresses IL-17-mediated skin inflammation and is genetically associated with psoriasis. *J Allergy Clin Immunol*. 2017;139(2):550-561. DOI:10.1016/J.JACI.2016.07.025 PMID: 27568078.
33. NCBI Reference SNP (rs) Report. Accesed: March 28, 2025. https://www.ncbi.nlm.nih.gov/snp/rs2910164
34. Jazdzewski K, Murray EL, Franssila K, Jarzab B, Schoenberg DR, De La Chapelle A. Common SNP in pre-miR-146a decreases mature miR expression and predisposes to papillary thyroid carcinoma. *Proc Natl Acad Sci U S A*. 2008;105(20):7269-7274. DOI:10.1073/pnas.0802682105 PMID: 18474871.
35. Yin Z, Cui Z, Ren Y, Xia L, Li H, Zhou B. MiR-146a polymorphism correlates with lung cancer risk in Chinese nonsmoking females. *Oncotarget*. 2016;8(2):2275. DOI:10.18632/ONCOTARGET.13722 PMID: 27911870.
36. Mohammed SR, Shaker OG, Mohammed AA, et al. Impact of miR-155 (rs767649 A>T) and miR-146a (rs57095329 A>G) polymorphisms in System Lupus Erythematosus susceptibility in an Egyptian cohort. *Eur Rev Med Pharmacol Sci*. 2021;25(3):1425-1435. DOI:10.26355/EURREV_202102_24850 PMID: 33629312.
37. Wang R, Wei A, Zhang Y, et al. Association between genetic variants of microRNA-21 and microRNA-155 and systemic lupus erythematosus: A case-control study from a Chinese population.

J Clin Lab Anal. 2022;36(7). DOI:10.1002/JCLA.24518 PMID: 35707883.

38. Ali MA, Shaker OG, Eid HM, Mahmoud EE, Ezzat EM, Gaber SN. Relationship between miR-155 and miR-146a polymorphisms and susceptibility to multiple sclerosis in an Egyptian cohort. *Biomed reports*. 2020;12(5):276-284. DOI:10.3892/BR.2020.1286 PMID: 32257191.
39. Shaker OG, Abdelaleem OO, Fouad NA, et al. MiR-146a and miR-155 polymorphisms in Egyptian patients with Behcet's disease. *Arch Med Sci*. 2021;18(6):1467-1474. DOI:10.5114/AOMS/105349 PMID: 36457982.
40. Elghouneimy MA, Ramadan MA, Farrag EA, et al. Impact of miR-155 rs767649 Polymorphism on Rheumatoid Arthritis Activity in Egyptian Patients. *Cureus*. 2023;15(11):e49297. DOI:10.7759/CUREUS.49297 PMID: 38351964.
41. Shaker OG, Abdelaleem OO, Fouad NA, et al. Association Between miR-155, Its Polymorphism and Ischemia-Modified Albumin in Patients with Rheumatoid Arthritis. *J Interferon Cytokine Res*. 2019;39(7):428-437. DOI:10.1089/JIR.2019.0001 PMID: 31009294.
42. Xie K, Ma H, Liang C, et al. A functional variant in miR-155 regulation region contributes to lung cancer risk and survival. *Oncotarget*. 2015;6(40):42781-42792. DOI:10.18632/ONCOTARGET.5840 PMID: 26543233.
43. Dezfuli NK, Adcock IM, Alipoor SD, et al. The miR-146a SNP Rs2910164 and miR-155 SNP rs767649 Are Risk Factors for Non-Small Cell Lung Cancer in the Iranian Population. *Can Respir J*. 2020;2020:8179415. DOI:10.1155/2020/8179415 PMID: 33294082.
44. Ji J, Xu M, Tu J, et al. MiR-155 and its functional variant rs767649 contribute to the susceptibility and survival of hepatocellular carcinoma. *Oncotarget*. 2016;7(37):60303-60309. DOI:10.18632/ONCOTARGET.11206 PMID: 27531892.
45. Wang S, Cao X, Ding B, et al. The rs767649 polymorphism in the promoter of miR-155 contributes to the decreased risk for cervical cancer in a Chinese population. *Gene*. 2016;595(1):109-114. DOI:10.1016/J.GENE.2016.10.002 PMID: 27717891.
46. Budu-Aggrey A, Bowes J, Loehr S, et al. Replication of a distinct psoriatic arthritis risk variant at the IL23R locus. *Ann Rheum Dis*. 2016;75(7):1417-1418. DOI:10.1136/ANNRHEUMDIS-2016-209290 PMID: 27016051.