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Article

Role of Interleukin-10 Promoter Gene Polymorphisms in Susceptibility to Systemic Lupus Erythematosus: Systematic Review

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Desi Oktariana[1*], Ade Rizki Putri Ratih[2], Phey Liana[1], Kemas Ya'kub Rahadiyanto[1], Ririn Eviningtyas[1], Gita Dwi Prasasty[3], Yuniza Yuniza[4], Hafizzanovian Hafizzanovian[4], Aseptianova Aseptianova[5]

[1]Department of Clinical Pathology, Department of Biomedical Science, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia
[2]Master of Biomedical Science Program, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia
[3]Department of Parasitology, Department of Biomedical Science, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia
[4]Department of Internal Medicine, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia
[5]Department of Biology Education, Faculty of Teacher Training and Education, Universitas Muhammadiyah Palembang, Palembang, Indonesia

Abstract. Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease characterized by multisystem inflammation that predominantly affects women of reproductive age. Genetic factors, particularly polymorphisms within the interleukin-10 (IL-10) promoter region, have been implicated in disease susceptibility through their influence on cytokine expression and immune regulation. This systematic review aimed to evaluate the association between IL-10 promoter polymorphisms and SLE susceptibility across different populations. A systematic literature search was conducted according to PRISMA guidelines using Google Scholar, PubMed, ScienceDirect, SagePub, and Wiley Online Library for studies published between 2005 and 2025. Eligible case-control studies investigating IL-10 promoter polymorphisms in SLE were included. Of 82 records identified, 12 studies met the eligibility criteria, comprising 2,462 patients with SLE and 3,274 healthy controls. Most studies reported significant associations between SLE susceptibility and the IL-10 promoter polymorphisms −1082A/G, −819C/T, and −592C/A. The GCC haplotype was the most consistently reported risk haplotype and was frequently associated with increased IL-10 expression and greater susceptibility to SLE. Overall, current evidence supports the contribution of IL-10 promoter polymorphisms to genetic susceptibility to SLE across diverse populations.

Corresponding Author :
Desi Oktariana
Department of Clinical Pathology, Department of Biomedical Science, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia
Email : desioktariana@fk.unsri.ac.id

1. Introduction

Systemic lupus erythematosus (SLE) is a complex, chronic autoimmune disorder that manifests as widespread inflammation affecting multiple organs and tissues, including the skin, kidneys, joints, and central nervous system [1]. The disease develops when the immune system cannot differentiate between self and non-self-antigens. This leads to the production of autoantibodies and immune complexes that damage tissues [2]. In Indonesia, the prevalence of SLE has increased in recent years, reaching approximately 1.3 million cases, with majority of patients being women of reproductive age [3]. According to the Hospital Information System (SIRS) in 2016, more than 858 hospitals reported cases of SLE across the country [3-4]. Globally, the prevalence reaching 3.4 million people worldwide, and 0.4 million newly diagnosed each year [5-6]. Highest incidence observed in Poland, United States, Barbados and China [5-6]. The female-to-male ratio of SLE ranges between 7:1 to 15:1, highlighting the strong influence of hormonal and genetic factors in disease expression [1],[7-8].

Although the etiology of SLE remains unclear, a combination of genetic, hormonal, and environmental factors has been implicated [9-11]. Among genetic contributors, polymorphisms within immune regulatory genes including those coding for cytokines play a pivotal role in determining individual susceptibility [12-13]. One of the most studied cytokines is interleukin-10 (IL-10), an anti-inflammatory cytokine that controls both innate and adaptive immune responses [14]. Interleukin-10 plays a dual role in SLE. It can suppress the production of pro-inflammatory cytokines and limit tissue damage, but it can also promote B-cell growth and autoantibody production—both of which drive disease progression [15-17]. Variations in the IL-10 gene promoter, especially at positions -1082, -819, and -592, can change transcriptional activity and cytokine expression levels [17-19]. These genetic variations may influence the balance between pro-inflammatory and anti-inflammatory immune responses in SLE.

Among the numerous polymorphic sites identified within the IL-10 promoter region, the −1082A/G, −819C/T, and −592C/A polymorphisms were selected as the primary focus because they are the three most extensively investigated functional variants in autoimmune diseases [15-17]. These polymorphisms form common promoter haplotypes (GCC, ACC, and ATA), which have been shown to influence transcriptional activity, IL-10 production, and immune regulation [17-19]. Consequently, these variants provide the strongest available evidence for evaluating the genetic contribution of IL-10 to SLE susceptibility across different ethnic populations.

Previous research across various populations shows inconsistent results about the link between IL-10 promoter polymorphisms and SLE susceptibility [20-22]. Some studies found significant connections between specific IL-10 haplotypes and increased disease risk, while others found no meaningful association [17-21]. Given these differences, a systematic review is necessary to summarize existing evidence and clarify how IL-10 promoter polymorphisms contribute to SLE susceptibility across different groups.

2. Materials and Methods

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure methodological clarity and reproducibility. The review process included four main stages: identification, screening, eligibility assessment, and inclusion of relevant studies [23]. This systematic review uses the PCO model: population/problem (P) refers to patients with systemic lupus erythematosus; comparison/control (C) refers to healthy patients; outcome (O) pertains to IL-10 gene allele/genotype or haplotype polymorphisms.

2.1. Eligibility Criteria

Studies were considered eligible for inclusion if the following criteria were fulfilled: (1) publication between 2005 and 2025; (2) investigation of IL-10 gene polymorphisms, the role of IL-10 in patients with systemic lupus erythematosus, or IL-10 expression levels in SLE; (3) involvement of human participants; and (4) availability in either English or Indonesian. Studies were excluded if categorized as laboratory-based experimental research, literature reviews, systematic reviews, meta-analyses, conference abstracts, or letters to the editor. Only clinical observational studies, specifically those utilizing a case-control design, were included.

2.2. Search Strategy

A thorough literature search was conducted using several databases, including Google Scholar, Pubmed/MEDLINE, ScienceDirect, SagePub, and Wiley Online Library. The search was carried out in October 2025. The following keywords and Boolean operators were used: "IL-10 polymorphism" OR "interleukin-10 SLE" OR "SLE polymorphism" AND "systemic lupus erythematosus.". Additional filters limited the results to peer-reviewed journal articles. The reference lists of relevant studies were also manually checked for additional eligible publications.

2.3. Data Extraction

All identified articles were imported into a reference manager to eliminate duplicates. Two reiewers screened the titles and abstracts independently to evaluate relevance based on the inclusion criteria. Full-text articles that met the criteria were then reviewed in detail. Data extracted from each study included:

- Author(s)
- Year of publication
- Country and population studied
- IL-10 polymorphism sites investigated
- Number of SLE patients and healthy controls
- Study design
- Main findings and statistical significance

2. 4. Study Selection

Initially, 82 records were identified across the five databases (Google Scholar, PubMed, ScienceDirect, SagePub, and Wiley Online Library). Forty-five were excluded due to duplication or failure to meet eligibility criteria. After reviewing titles and abstracts, 37 studies were selected for full-text review, and 12 ultimately met all inclusion requirements. The PRISMA flow diagram summarizing the selection process is presented in Figure 1.

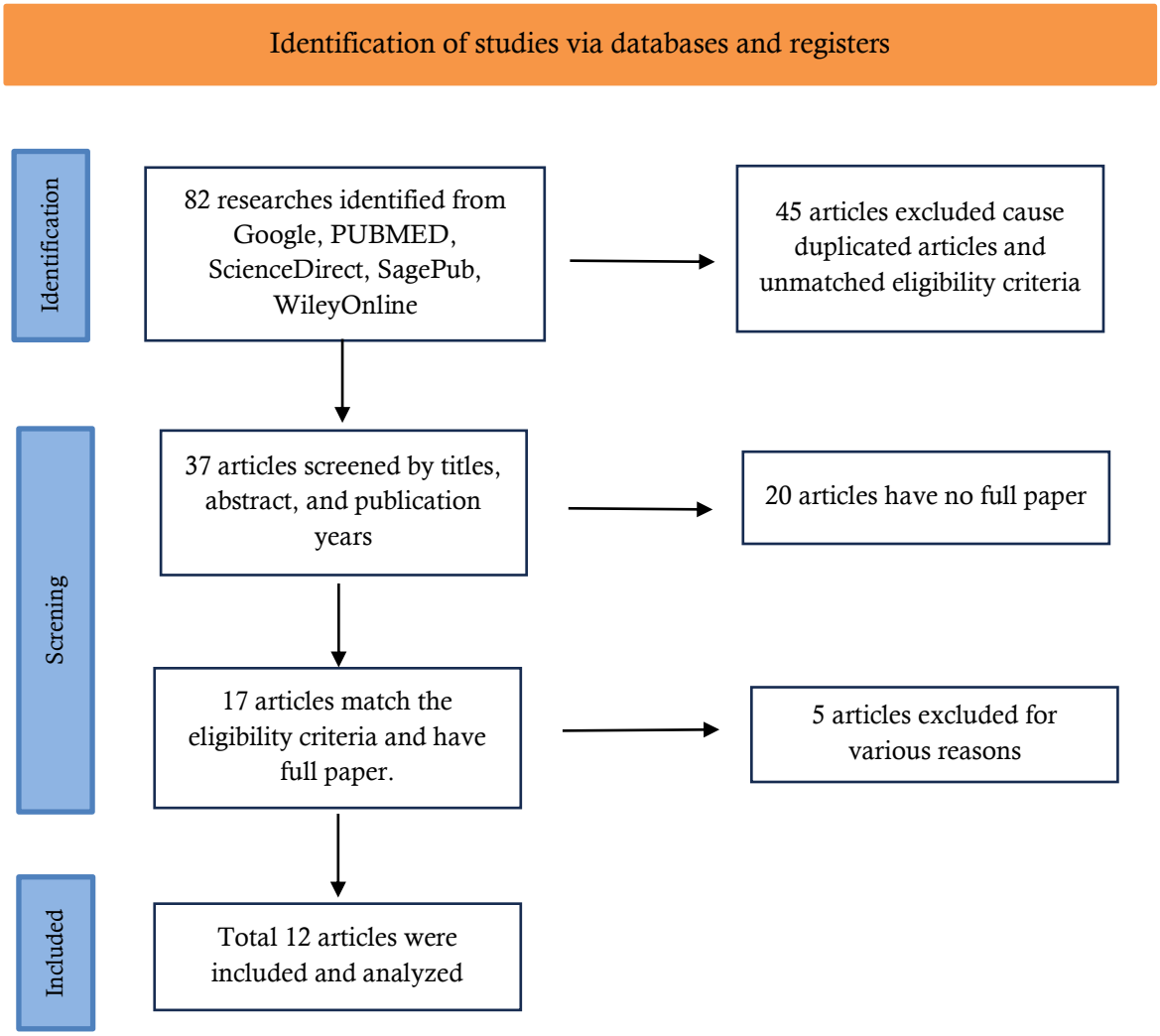

Figure 1. Systematic flow diagram PRISMA

3. Results and Discussion

3.1. Study Characteristics

The 12 studies included in the review covered a wide range of geographical regions and ethnic backgrounds, representing populations from Asia (China, India, Thailand, Iran), Europe (Poland, Spain, Germany), and Africa (Egypt). All studies used a case-control design to compare individuals diagnosed with systemic lupus erythematosus to healthy controls. This design ensured consistency across studies for interpretation. In total, the studies involved 2,462 SLE cases and 3,274 controls, providing a substantial dataset for examining genetic connections across diverse populations. This broad representation enhances the generalizability of the findings and emphasizes the global significance of IL-10 promoter polymorphisms as potential risk factors for SLE.

The promoter polymorphisms studied most often included −1082A/G, −819C/T, and −592C/A, while several studies also looked at less frequently analyzed variants like −2849G/A and 4529A/G. These genetic variations are known to modify promoter function and regulate IL-10 transcriptional activity, which can change downstream cytokine expression. Such changes may lead to an imbalance between pro-inflammatory and anti-inflammatory signaling, a key aspect of SLE

immunopathogenesis. Patterns across studies suggest that these promoter variants may affect susceptibility by modulating IL-10–mediated immune pathways, supporting their importance as genetic markers in autoimmune disease research. The findings from the data extraction are presented in Tables 1 and 2.

Table 1. Description of various variable study

Study (years)	Population	Sites Polymorphisms	SLE	Controls	Study Design
Emerah AA et al (2015) [24]	Egyptian	1082A/G	54	27	Case Control
Wang GH et al (2020) [8]	Chinese	1082A/G, 592C/A, 819C/T, 4529A/G	391	785	Case Control
Zak-Golab et al (2024) [18]	Polish	1082A/G, 819T/C, 592A/C	67	67	Case Control
Umare V et al (2020) [17]	Indian	1082A/G, 819T/C, 592C/A	200	201	Case Control
Rzeszotarska et al (2022) [20]	Polish	592C/A, 1082A/G	230	361	Case Control
Rosado S et al (2008) [25]	Spanish	1082G/A, -819C/T and -592C/A	80	151	Case Control
Sobkowiak et al (2009) [26]	Polish	627C/A, 854C/T and 1117G/A	103	300	Case Control
Schotte H et al (2014) [27]	German caucasian	2849 G/A, 1082 A/G, 819 T/C and 592 C/A	210	160	Case Control
Wang B et al (2017) [21]	Chinese	1082G/A, 819C/T, 592C/A	579	673	Case Control
Zhang et al (2017) [28]	Chinese	1082 A/G, -819 T/C, -592 A/C	237	259	Case Control
Mohammadi et al (2019) [29]	Iranian	1082 A/G, -819 T/C, -592 A/C	116	131	Case Control
Hirankarn et al (2006) [30]	Thai	1082 A/G, -819 T/C, -592 A/C	195	159	Case Control

Table 1 offers a brief overview of the populations, sites of polymorphism, and the methodologies used in the studies reviewed. Research conducted in Asia, especially in China and India, showed significantly larger sample sizes compared to studies from Europe and Africa. For instance, the study by Wang GH et al. involved 391 patients and 785 controls [8], while the Egyptian research by Emerah AA et al. included only 54 cases and 27 controls [24]. The −1082A/G locus was the most frequently studied, appearing in nearly all of the included research. This recurrent focus underscores its potential significance in the regulation of IL-10 expression.

Variations found in this area may have a direct impact on the binding affinity of transcriptional nuclear factors, thus influencing cytokine secretion. Conversely, infrequent analysis of −819C/T and −592C/A indicates their secondary yet complementary functions. Variations in sample size, population genetics, and study scope lead to the heterogeneity observed in research findings. Table 1, however, shows a pattern that keeps coming up: IL-10 promoter polymorphisms, especially at −1082A/G, seem to be more common in SLE patients. This suggests that people with SLE may have a genetic predisposition that is shared across populations.

Tabel 2. Result main findings and conclusion the study

Study (years)	Country	Findings	p value
Emerah AA et al (2015) [24]	Egypt	Associated with genotype AA	0.029
Wang GH et al (2020) [8]	China	Associate with G and T alleles	$p < 0.05$
Zak-Golab et al (2024) [18]	Poland	No clinical significance difference	$p > 0.05$*
Umare V et al (2020) [17]	India	Associated with haplotype GCA	0.022
Rzeszotarska et al (2022) [20]	Poland	Associated with polymorphism sites 1082A/G	0.042
Rosado S et al (2008) [25]	Spain	Associated with haplotype GCC	0.02
Sobkowiak et al (2009) [26]	Poland	Associated with GCC genotype	0.0022
Schotte H et al (2014) [27]	German	No significant difference	$p > 0.05$*
Wang B et al (2017) [21]	China	Associated with IL-10-1082G/A, but no significant differences with position -819 C/T and -592 C/A	$p < 0.001$ $p > 0.05$*
Zhang et al (2017) [28]	China	Associated with AG genotype, GCC carriers and -1082 A/G	$p < 0.05$
Mohammadi et al (2019) [29]	Iran	Associated with GG genotype of −1082, polymorphism and CC genotype in −819 region	0.046 0.034
Hirankarn et al (2006) [30]	Thailand	Associated with ACC haplotype	0.002

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease characterized by a wide range of immunological irregularities and clinical presentations [1]. Despite extensive research over several decades, the precise pathogenic networks that facilitate the condition's development remain inadequately defined [8]. Current scientific understanding indicates that systemic lupus erythematosus (SLE) arises from a multifactorial interplay wherein genetic predisposition and environmental exposures collectively affect an individual's susceptibility to disease onset. A range of determinants has been suggested, encompassing inherited variations in immune-regulating genes, endocrine factors such as fluctuations in sex hormones, ultraviolet radiation, the administration of specific pharmacological agents, and infectious triggers that can alter immune activity [19],[31]. Our review synthesizes data from twelve peer-reviewed publications, comprising a total sample of 2,462 patients diagnosed with SLE and 3,274 healthy controls, thereby offering a comprehensive comparative framework for the interpretation of pertinent risk factors.

A consistent epidemiological finding is that SLE predominantly affects women of reproductive age. Although sex hormones and X chromosome-linked immune regulation contribute to this susceptibility, the present review focuses specifically on IL-10 promoter polymorphisms because these variants directly influence cytokine expression and immune homeostasis. Therefore, genetic variation within the IL-10 promoter region may represent one of the molecular mechanisms underlying the increased risk of SLE across different populations [24],[26].

3.2. Association between IL-10 Gene Polymorphisms and SLE Susceptibility

Cytokines are an important part of the humoral immune system and are important for controlling how cells talk to each other during immune responses. These molecules are crucial for coordinating numerous immunological processes, encompassing the activation, differentiation, and maturation of diverse immune cell populations [13]. Cytokines can be broadly classified into pro-inflammatory mediators, which enhance immune activation, and anti-inflammatory mediators, which serve to restrict excessive immune responses and preserve immunological equilibrium. Interleukin-10 (IL-10)

is one of the most important cytokines that modulates the immune system. It is well known for its ability to stop inflammatory signaling and control the strength of immune activity. The IL-10 cytokine is mainly known for its anti-inflammatory effects, which stop the production of pro-inflammatory cytokines like IL-1β, IL-6, and TNF-α [15-16]. However, IL-10's dual role of promoting autoimmunity and suppressing inflammation emphasizes its intricate regulatory involvement in the pathophysiology of systemic lupus erythematosus. Initially acting as a compensatory anti-inflammatory strategy, elevated IL-10 expression might eventually contribute to the duration of the illness by increasing the generation of autoantibodies [15-16].

The production of interleukin-10 is known to be influenced, to a considerable extent, by genetic factors [18]. The IL-10 gene, located on chromosome 1q31–q32, has an important role in regulating the level of IL-10 expression [8]. Variations within its promoter region may affect the binding affinity of transcription factors to regulatory elements, which in turn can influence the initiation of gene transcription [32]. These polymorphisms may lead to changes in mRNA expression and subsequently contribute to altered cytokine production [33]. Such regulatory alterations have been linked to an increased susceptibility to autoimmune conditions. When IL-10 expression is not properly maintained, the balance between pro-inflammatory and anti-inflammatory pathways can become disrupted. In this context, promoter polymorphisms are thought to affect IL-10 transcription primarily through their impact on transcription factor binding [29]. In addition, excessive IL-10 expression may reduce the ability of macrophages to effectively clear apoptotic cells. As a result, secondary necrotic debris (SNECs) can accumulate and act as autoantigens, further stimulating immune responses and contributing to ongoing inflammation and tissue damage [33]

Overall, the included studies consistently suggest that IL-10 promoter polymorphisms are associated with increased susceptibility to Systemic Lupus Erythematosus (SLE), although the strength of the associations varies across different populations. In most cases, these associations were examined using haplotype-based analyses rather than focusing on individual single-nucleotide polymorphisms. A haplotype represents a combination of genetic variants inherited together within an individual. In this synthesis, the GCC haplotype was the variant most consistently associated with increased IL-10 production. Similar findings were reported by Rosado et al., Sobkowiak et al., and Zhang et al., all of whom identified a clear relationship between the GCC haplotype and a higher susceptibility to SLE [25-28].

3.3. Associated -1082A/G site Polymorphisms gene IL-10

Interindividual differences in IL-10 production are largely attributed to genetic variation within the promoter region of the IL-10 gene. In this study, polymorphisms at the -1082A/G locus were most frequently associated with disease risk, with an estimated occurrence of 42.8% across the included studies. Several reports have highlighted specific genotypes and haplotypes—such as GCC, ACC, and GCA—that are linked to increased IL-10 expression and a higher risk of SLE [18],[20].

The –1082 A/G polymorphism is located within a regulatory region of the IL-10 promoter that is thought to influence transcriptional activity by affecting transcription factor binding sites and other cis-regulatory elements (CRE) [24],[34]. Variations at this position may alter promoter function, resulting in changes in cytokine expression that contribute to the immune imbalance observed in SLE.

Consistent with this, Rzeszotarska et al. reported an association between the -1082A/G polymorphism and elevated serum IL-10 levels in a Polish cohort, suggesting a role in immune dysregulation. Likewise, Umare et al. identified a significant relationship between the GCA haplotype and disease susceptibility in an Indian population. However, not all studies have shown similar findings. For example, Zak-Golab et al. and Schotte et al. did not observe significant associations in European populations, which may reflect differences in sample size, genetic background, or environmental influences [17-20].

3.5. Comparative Findings among Populations

Comparative analyses suggest that ethnic background influences both the distribution and functional impact of IL-10 polymorphisms. Asian populations generally show stronger associations, particularly for the −1082G allele, whereas findings in European and African populations are less consistent.

Variation in the strength of association between IL-10 polymorphisms and SLE susceptibility across populations likely reflects underlying genetic diversity [19]. Overall, studies from Asian cohorts tend to demonstrate stronger correlations compared to those from European populations. These differences may be influenced by allele frequency patterns, environmental exposures, and gene–environment interactions. In addition, haplotypes associated with higher IL-10 expression seem to occur more frequently in Asian populations, further supporting the idea that population-specific genetic backgrounds contribute to disease risk.

A more detailed look at regional patterns highlights several notable findings. In Asian populations, particularly in studies from China and India, the association between IL-10 promoter polymorphisms and SLE risk is consistently reported. For example, Wang GH et al. and Wang B et al. identified significant relationships between specific alleles, including G and T variants, and increased susceptibility. Similarly, Umare V et al. reported that the GCA haplotype was strongly associated with disease risk, with the relatively high frequency of the G allele potentially contributing to this pattern [8],[17],[21].

In European populations, the findings are more variable. While Rzeszotarska et al. observed that the −1082A/G polymorphism was linked to higher IL-10 serum levels in a Polish cohort, other studies, such as those by Zak-Golab et al. and Schotte et al., did not find statistically significant associations [18],[20]. These inconsistencies may be attributed to heterogeneity among European subpopulations, differences in sample size, or environmental factors such as ultraviolet exposure and dietary habits.

Evidence from Middle Eastern and African populations also point to a meaningful relationship between IL-10 polymorphisms and SLE. Studies conducted in Iran [29] and Egypt [24] reported that the GG genotype at −1082 and the CC genotype at −819 were associated with both increased disease risk and higher IL-10 expression. These findings support the notion that elevated IL-10 levels, despite their anti-inflammatory role, may paradoxically contribute to autoimmunity by promoting B-cell activation and autoantibody production.

3.6. Strength and Limitations

Although most included studies suggest an association between IL-10 promoter polymorphisms and increased susceptibility to SLE, several limitations should be considered. Considerable heterogeneity existed among the included studies in terms of ethnicity, sample size, genotyping methods, and genetic models, which may have contributed to the variability of the findings. Because this review was conducted as a qualitative systematic review rather than a meta-analysis, statistical heterogeneity (e.g., I^2) was not assessed. In addition, differences in the polymorphisms investigated and outcome reporting precluded quantitative data synthesis.

Another limitation is the limited consideration of environmental factors, such as ultraviolet exposure and infection history, which may influence SLE susceptibility. Future studies involving larger multicenter populations with standardized methodologies are needed to better clarify the relationship between IL-10 promoter polymorphisms and SLE.

4. Conclusion

Overall, this systematic review highlights a consistent association between IL-10 promoter polymorphisms and increased susceptibility to Systemic Lupus Erythematosus across diverse populations. These genetic variations appear to influence cytokine regulation and immune balance, underscoring the role of IL-10 as an important contributor to lupus predisposition. In particular, haplotypes such as GCC and GCA have been repeatedly associated with higher IL-10 expression and

more pronounced autoimmune activity. Despite these findings, the evidence remains influenced by variability across studies. Therefore, further well-designed, multicenter investigations involving diverse populations along with integrated analyses of genetic and environmental factors are needed to better clarify the underlying mechanisms and establish more definitive causal relationships.

References

[1] Garcia-Rios, P., Pecci-Lloret, M. P., and Onate-Sanchez, R. E. (2022). Oral manifestations of systemic lupus erythematosus: A systematic review. *International Journal of Environmental Research and Public Health*, 19, 1–12.

[2] Pisetsky, D. (2023). Pathogenesis of autoimmune disease. *Nature Reviews Nephrology*, 19(8), 509–524.

[3] Tanzilia, M. F., Tambunan, B. A., and Dewi, D. N. S. S. (2021). Literature review: Pathogenesis and diagnosis of systemic lupus erythematosus. *Syifa' Medika*, 11(2), 139–164.

[4] Pusdatin. (2017). *Situasi lupus di Indonesia*. *Infodatin: Pusat Data dan Informasi Kementerian Kesehatan RI*. Accessed October 10, 2025.

[5] Dai, X., Fan, Y., and Zhao, X. (2025). Systemic lupus erythematosus: Updated insights on the pathogenesis, diagnosis, prevention and therapeutics. *Signal Transduction and Targeted Therapy*, 10(102), 1–51.

[6] Tian, J., Zhang, D., Yao, X., Huang, Y., and Lu, Q. (2022). Global epidemiology of systemic lupus erythematosus: A comprehensive systematic analysis and modelling study. *Annals of the Rheumatic Diseases*, 81, 1–6.

[7] Thomas, R., and Jawad, A. S. (2022). Systemic lupus erythematosus: Rarer in men than women but more severe. *Trends in Urology & Men's Health*, 13(5), 11–14.

[8] Wang, G. H., Zuo, T., and Zuo, Z. C. (2020). Impact of IL-10 gene polymorphisms and its interaction with environment on susceptibility to systemic lupus erythematosus. *International Journal of Immunopathology and Pharmacology*, 34, 1–7.

[9] Weinstein, A., Alexander, R. V., and Zack, D. J. (2021). A review of complement activation in SLE. *Current Rheumatology Reports*, 23(16), 1–8.

[10] Aswin, A., Riastiti, Y., and Rahmah, Y. (2023). Risk factors for systemic lupus erythematosus (SLE) in East and North Kalimantan. *Jurnal Kedokteran Mulawarman*, 10(3), 129–137.

[11] Woo, J. M. P., Parks, C. G., Jacobsen, S., Costenbader, K. H., and Bernatsky, S. (2022). The role of environmental exposures and gene–environment interactions in the etiology of systemic lupus erythematosus. *Journal of Internal Medicine*, 291(6), 755–778.

[12] Barliana, M. I., Afifah, N. N., Amalia, R., Hamijoyo, L., and Abdullah, R. (2022). Genetic polymorphisms and the clinical response to systemic lupus erythematosus treatment towards personalized medicine. *Frontiers in Pharmacology*, 13, 1–14.

[13] Oktariana, D., Saleh, I., Hafy, Z., Liberty, I. A., Salim, E. M., and Legiran, L. (2022). The role of interleukin-10 in leprosy: A review. *Indian Journal of Leprosy*, 94(2), 125–134.

[14] Bolouri, N., Akhtari, M., Farhadi, E., Mansouri, R., and Faezi, S. T. (2022). Role of the innate and adaptive immune responses in the pathogenesis of systemic lupus erythematosus. *Inflammation Research*, 71, 537–544.

[15] Richter, P., Macovei, L. A., Rezus, C., Boiculese, V. L., Buliga-Finis, O. N., and Rezus, E. (2025). IL-10 in systemic lupus erythematosus: Balancing immunoregulation and autoimmunity. *International Journal of Molecular Sciences*, 26(7), 3290.

[16] Biswas, S., Bieber, K., and Manz, R. A. (2022). IL-10 revisited in systemic lupus erythematosus. *Frontiers in Immunology*, 13, 1–6.

[17] Umare, V., Pradhan, V., Dadheech, S., Rajadhyaksha, A., Ghosh, K., and Nadkarni, A. (2020). Clinical implications of IL-10 promoter polymorphisms on disease susceptibility in Indian SLE patients. *Lupus*, 29(6), 587–598.

[18] Zak-Gołab, A., Cieślik, P., Siekiera, U., Kuśmierz, D., Hrycek, A., and Holecki, M. (2024). The impact of the IL-10 gene polymorphism on mRNA expression and IL-10 serum concentration in Polish lupus patients. *International Journal of Molecular Sciences*, 25(10), 5511.

[19] Liu, P., Song, J., Su, H., Li, L., Lu, N., Yang, R., and Peng, Z. (2013). IL-10 gene polymorphisms and susceptibility to systemic lupus erythematosus: A meta-analysis. *PLoS ONE*, 8(7).

[20] Rzeszotarska, E., Sowinska, A., Stypinska, B., Lutkowska, A., Felis-Giemza, A., Olesinska, M., Puszczewicz, M., Majewski, D., Jagodzinski, P. P., Haładyj, E., and Paradowska-Gorycka, A. (2022). IL-1β, IL-10 and TNF-α polymorphisms may affect systemic lupus erythematosus risk and phenotype. *Clinical and Experimental Rheumatology*, 40(9), 1708–1717.

[21] Wang, B., Lu, J. S., Yang, X. K., Yuan, F. F., Wang, H., Lv, T. T., Fan, Y. G., and Ye, D. Q. (2017). Association of single nucleotide polymorphisms and haplotypes of the interleukin-10 5′ flanking region with systemic lupus erythematosus susceptibility in Han Chinese. *International Journal of Clinical and Experimental Pathology*, 10(2), 2156–2162.

[22] Grk, M., Miskovic, R., Jeremic, I., Basaric, M., Dusanovic Pjevic, M., Jekic, B., Miljanovic, D., Lazarevic, I., Despotovic, A., Cirkovic, A., and Banko, A. (2023). Association of IL10RA, IL10RB, and IL22RA polymorphisms/haplotypes with susceptibility to and clinical manifestations of SLE. *International Journal of Molecular Sciences*, 24, 11292.

[23] Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., and Chou, R. (2021). The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *Systematic Reviews*, 10(89), 1–9.

[24] Emerah, A. A., Mohamed, K. F., Elbadawy, N. E., and Rashad, M. H. (2015). Effects of interleukin-10 gene polymorphism on clinical diversity and activity of systemic lupus erythematosus. *The Egyptian Rheumatologist and Rehabilitation*, 42, 49–54.

[25] Rosado, S., Rua-Figueroa, I., Vargas, J. A., Garcia-Laorden, M. I., Losada-Fernandez, I., Martin-Donaire, T., Perez-Chacon, G., Rodriguez-Gallego, C., Naranjo-Hernandez, A., Ojeda-Bruno, S., and Citores, M. J. (2008). Interleukin-10 promoter polymorphisms in patients with systemic lupus erythematosus from the Canary Islands. *International Journal of Immunogenetics*, 35, 235–242.

[26] Sobkowiak, A., Lianeri, M., Wudarski, M., Lacki, J. K., and Jagodzinski, P. P. (2009). Genetic variation in the interleukin-10 gene promoter in Polish patients with systemic lupus erythematosus. *Rheumatology International*, 29, 921–925.

[27] Schotte, H., Willeke, P., Becker, H., Poggemeyer, J., and Gaubitz, M. (2014). Association of extended interleukin-10 promoter haplotypes with disease susceptibility and manifestations in German patients with systemic lupus erythematosus. *Lupus*, 23, 378–385.

[28] Zhang, J., Yang, S., Zhu, Y., Li, Y., Sun, J., Zhang, H., and Gui, M. (2017). Association of interleukin-10 promoter haplotypes with systemic lupus erythematosus susceptibility in Han Chinese. *International Journal of Clinical and Experimental Pathology*, 10(6), 7162–7168.

[29] Mohammadi, S., Saghaeian Jazi, M., Zare Ebrahimabad, M., Eghbalpour, F., Abdolahi, N., Tabarraei, A., and Yazdani, Y. (2019). Interleukin 10 gene promoter polymorphisms (rs1800896, rs1800871 and rs1800872) and haplotypes are associated with the activity of systemic lupus erythematosus and IL10 levels in an Iranian population. *International Journal of Immunogenetics*, 46, 20–30.

[30] Hirankarn, N., Wongpiyabovorn, J., Hanvivatvong, O., Netsawang, J., Akkasilpa, S., Wongchinsri, J., Hanvivadhanakul, P., Korkit, W., and Avihingsanon, Y. (2006). The

synergistic effect of Fc gamma receptor IIa and interleukin-10 genes on the risk of developing systemic lupus erythematosus in the Thai population. *Genes and Immunity*, 7(5), 399–406.

[31] Catalina, M. D., Owen, K. A., Labonte, A. C., Grammer, A. C., and Lipsky, P. E. (2020). The pathogenesis of systemic lupus erythematosus: Harnessing big data to understand the molecular basis of lupus. *Journal of Autoimmunity*, 110, 102359.

[32] Oktariana, D., Argentina, F., Hafy, Z., Salim, E. M., Kurniati, N., Rahadiyanto, K. Y., and Lusiana, E. (2021). Association of −819 T/C IL-10 gene promoter polymorphisms with susceptibility to leprosy in South Sumatera, Indonesia. *Leprosy Review*, 92(2), 162–169.

[33] Biermann, M. H., Boeltz, S., Pieterse, E., Knopf, J., Rech, J., Bilyy, R., Van der Vlag, J., Tincani, A., Distler, J. H., Krönke, G., and Schett, G. A. (2018). Autoantibodies recognizing secondary necrotic cells promote neutrophilic phagocytosis and identify patients with systemic lupus erythematosus. *Frontiers in Immunology*, 9, 989.

[34] Diamanti, K., Umer, H. M., Kruczyk, M., Dabrowski, M. J., and Cavalli, M. (2016). Maps of context-dependent putative regulatory regions and genomic signal interactions. *Nucleic Acids Research*, 44(19), 9110–9120.