Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 32s (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

Molecular Genetic And Immunological Diagnostic Markers Of Atopic Dermatitis

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Cite this paper as: Gulmira R. Razikova, (2025) Molecular Genetic And Immunological Diagnostic Markers Of Atopic Dermatitis. *Journal of Neonatal Surgery*, 14 (32s), 3164-3168.

ABSTRACT

160 patients with various forms of atopic dermatitis aged 3 to 62 years who were under observation at the Republican Specialized Center for Dermatovenerology and Cosmetology were examined.The aim of the study was to identify early the molecular genetic and immunological mechanisms of atopic dermatitis development and to improve the diagnosis. Based on a clinical, immunological and molecular genetic examination of patients with atopic dermatitis, the domestic "Hepaprot-Neo" 0.45 included T330G of the IL-2 gene and 2258G>A of toll-like receptor genes of the TLR2 gene for complex treatment, taking into account allelic variants, based on the fact that an individualized pathogenetic treatment technique has been developed, which is characterized by the appointment of a drug that stabilizes the hepatoprotective membrane and enhances immunity.

Keywords: *atopic dermatitis, atopic dermatitis marker genes, topical glucocorticosteroids, atopic syndrome.*

1. INTRODUCTION

Relevance of the problem. In the world, atopic dermatitis (AD) is still a global problem of the 21st century, due to the steady growth among the population, especially among children and adult patients. According to world statistics, approximately 7.1 to 27.4% of the population suffers from the disease, and the increase in incidence can be traced depending on various factors, both external and internal. According to the WHO, "... in recent years, cases of combined forms of respiratory allergic diseases and AD "dermatorespiratory syndrome" have become more frequent among children. The course of the disease in adults is thus expressed by the most persistent severe course of the disease, contributing to the development of complicated forms of dermatosis - the "atopic triad" or "severe atopic syndrome", thereby requiring improvement in the effectiveness of early diagnosis, prevention and treatment of blood pressure.

Comprehensive reforms are being carried out in our country to develop and bring the medical system in line with international standards, in particular, to prevent various skin diseases that occur in children and adults. The comprehensive measures to radically improve the healthcare system set out the tasks "... to increase the efficiency, quality and accessibility of medical care to the population, as well as to create a system of medical standardization, high-tech methods of diagnosis and treatment, promotion of a healthy lifestyle and disease prevention through the creation of effective models of medical examinations ...". In this regard, the priority remains early diagnosis, the development of effective treatment methods, and the prevention of the development of complicated forms of allergic skin diseases.[6].

The purpose of the study. early detection of the molecular genetic and immunological mechanisms of atopic dermatitis development and improved diagnosis.

Peripheral blood and blood serum were used as **the subject of the study.**

Material and research methods. The study used general clinical, immunological, molecular genetic and statistical research methods.

The results and discussion. Based on molecular genetic studies of atopic dermatitis, interaction with polymorphic variants of toll-like receptor 2258G>A of the TLR2 gene and allelic variants of the interleukin class T1237S gene, which play a key role in determining the clinical variants and severity of atopic dermatitis, has been established; in patients with atopic dermatitis, the level of pro-inflammatory (IL-2) and anti-inflammatory (IL-10) cytokines increased by 4.8 and 1.8 times with increasing severity of dermatosis against the background of hyperproduction of total immunoglobulin E, which is confirmed by the decompensatory reaction of cytokines.

It has been proven that with heterozygous and homozygous polymorphism of the T/G and G/G genotypes of negative allelic variants of the IL-2 gene in patients with atopic dermatitis, compared with positive T/T genotypes of this gene, the levels of the total immunoglobulin E index and the proinflammatory cytokine IL-2 increased sharply to 1.1-1.3 times;

based on the method of predicting the risk of developing severe forms of atopic dermatitis, taking into account the polymorphism genotypes of the TLR9 (rs5743836) T1237S gene and TLR2 2258G>A (Arg753Gln) gene;

polymorphism T330G of the IL-2 gene (rs2069762) and polymorphisms 2258G>A (Arg753Gln) of the TLR2 gene and T1237C of the TLR9 gene (rs5743836) are substantiated as a genetic marker of predisposition to allergic rhinitis combined with atopic dermatitis;

based on a clinical, immunological and molecular genetic examination of patients with atopic dermatitis, the domestic "Hepaprot-Neo" 0.45 included T330G of the IL-2 gene and 2258G>A of toll-like receptor genes of the TLR2 gene for complex treatment, taking into account allelic variants, based on the fact that an individualized pathogenetic treatment technique has been developed, which is characterized by the appointment of a drug that stabilizes the hepatoprotective membrane and enhances immunity.

It has been established that the association of polymorphisms of toll-like receptors 2258G>A of the TLR2 gene and T1237C of the TLR9 gene, as well as interleukins T330G of the IL2 gene, which play a key role in determining the severity, plays a role in the mechanism of development of clinical variants of the course of AD.

The practical significance of the research results lies in the development of a molecular genetic method for predicting severe clinical forms of dermatorespiratory syndrome in patients with atopic dermatitis, taking into account the determination of genotypes of the class of toll-like receptors TLR2 and TLR9 and interleukin T330G of the IL2 gene, the development of a new method of pathogenetic therapy characterized by the appointment of the domestic drug "Hepaprot–Neo" against the background of complex therapy contributed to an increase in therapeutic efficacy of 64.8% and a 3.9-fold reduction in the number of relapses. During budesonide therapy, it was noted that in the study the GCS dose was 83% lower, despite the fact that patients were given complete freedom regarding the frequency of use of drugs as needed. A comparative analysis of ELISA studies of cytokine status and total IgE in patients with AD with dermatorespiratory syndrome showed a pronounced hyperproduction of the proinflammatory cytokine IL-2 by 5.8 times compared with the control group, and by 1.2 times compared with the group of patients with AD without dermatorespiratory syndrome and averaged 20.9±1.0 pg/ml ($P<0.05$). Whereas the level of IL-10 averaged 9.7±0.07 pg/ml, which was 1.03 times higher than in patients without dermatorespiratory syndrome and 1.9 times higher than in healthy individuals ($P<0.05$). Increased levels of IL-2 and IL-10 in AD patients with dermatorespiratory syndrome indicate activation of the autoimmune process, accompanied by the addition of bacterial or fungal / viral infection in the body.

An analysis of clinical and immunological studies showed that in patients with blood pressure, with an increase in the severity of dermatosis, there is a decompensatory reaction of pro- and anti-inflammatory cytokines against the background of hyperproduction of total immunoglobulin E, characterized by an increase in IL-2 and IL-10 levels by 4.8 and 1.8 times compared with those of healthy individuals, respectively, and a gradual decrease in IL production-2 - 1.4 times and IL-10 - 1.07 times compared with indicators of mild severity of dermatosis. The data obtained indicates the development of optimal methods of immunocorrection in patients with atopic dermatitis. To assess the detectability of allelic variants and genotypes of the studied genes, the patients were divided into 3 subgroups:

1) subgroup 1.1 – patients with atopic dermatitis only (AD, n=53),

2) subgroup 1.2 – patients with AD and allergic rhinitis (AD+AR, n=30),

3) subgroup 1.3 – patients with AD and bronchial asthma (AD+BA, n=17).

A comparative analysis of the frequency of polymorphic alleles and genotypes of candidate genes was carried out in these groups and subgroups.

Table 1 Frequency of alleles and genotypes of the rs5743708 (Arg753Gln) TLR2 gene polymorphism in groups of atopic patients and controls

№	Group	Frequency of alleles				Frequency of alleles					
		G (Arg)		A (Gln)		G/G (Arg/Arg)		G/A (Arg/Gln)		A/A (Gln/Gln)	
		n	%	n	%	n	%	n	%	n	%
1	Basic group, n=100	186	93,00	14	7,00	86	86,00	14	14,00	0	0

1.1	Atopic dermatitis n=53	97	91,51	9	8,49	44	83,02	9	16,98	0	0
1.2	Atopic dermatitis + allergic rhinitis, n=30	59	98,33	1	1,67	29	96,67	1	3,33	0	0
1.3	Atopic dermatitis + bronchial asthma n=17	30	88,24	4	11,76	13	76,47	4	23,53	0	0
2	The control group, n=98	189	96,43	7	3,57	91	92,86	7	7,14	0	0

Our study of the frequency of distribution of alleles of the rs5743708 polymorphism of the TLR2 gene (2258G/A or Arg753Gln) in a sample of patients in the main group and in the population sample (control) showed that the mutant allele "A" was significantly more common in patients with atopy than in the control (7.0% and 3.6%, respectively; $\chi 2=2.32$; $p<0.2$; OR=2.03; 95%CI 0.816-5.065); the frequency of the "wild" allele "G" had indicators without a significant predominance of the control group over the group of patients (96.4% and 93.0%, respectively; $\chi 2=3.32$; $p<0.2$; OR=0.49; 95%CI 1.226-0,198). The data obtained in our study, despite the high odds ratio (OR=2.03), indicate that there is no association between allele "A" of polymorphism rs5743708 (Arg753Gln) of the TLR2 gene and atopic pathology.

Thus, the data of our study showed the association of the unfavorable variant allele "A" of the rs5743708 polymorphism of the TLR2 gene, leading to the replacement of Arg by Gln at position 753 of the amino acid sequence, with the development of bronchial asthma in the presence of atopic dermatitis in the patient. We found that the risk of developing this secondary atopic pathology in the presence of a variant polymorphism allele in the genome is increased 3.6 times (OR=3.6). The obtained result also indicates that the heterozygous genotype of the rs5743708 polymorphism of the TLR2 gene is a genetic determinant that determines the formation of bronchial asthma against the background of atopic dermatitis, and the carriage of the G/A genotype is a predisposition factor for the development of this pathology, increasing its risk by 4 times (OR=4.0).

Whereas, a study of the frequency of distribution of alleles of the TLR9 polymorphism T1237C (rs5743836) in a sample of patients in the main group and in the population sample (control) showed that the mutant allele "C" occurred in patients with atopy in the main group with almost the same frequency as in the control group (9.5% and 10.2%, respectively; $\chi 2=0.06$; $p<0.9$; OR=0.924; 95%CI 0.477-1.789); the frequency of the "wild" T allele also had similar values (respectively, 90.5% and 89.8%; $\chi 2=0.06$; $p<0.9$; OR=1.083; 95%CI2.096-0,559). The data obtained in our study indicate the absence of an association between the variant allele "C" of polymorphism T1237C (rs5743836) of the TLR9 gene and atopic pathology. (Table 2).

Table 2 Comparative assessment of the expected and observed heterozygosity frequencies of the TLR9 t1237 C (rs5743836) polymorphism in the studied groups of patients with atopy and controls

Groups	**H_o**	**H_e**	**D ***
1. Basic group	0,19	0,17	0,105
1.1. AD	0,19	0,17	0,104
1.2. AD + AR	0,03	0,03	0,017
1.3. AD + BA	0,47	0,36	0,308
2. The control group	0,18	0,18	0,002

Note: D=(Ho–He)/He, where D is the relative deviation of the expected heterozygosity from the observed one, Ho is the observed heterozygosity, and He is the expected heterozygosity.

Based on equation XB, in the population control group, the theoretically expected frequency of homozygous genotype T/T polymorphism T1237C (rs5743836) of the TLR9 gene was 0.81, heterozygous genotype T/C was 0.18, and homozygous for the mutant allele genotype C/C was 0.01. The values of the observed frequency of polymorphism genotypes were, respectively, 0.81 for T/T, 0.18 for T/S and 0.01 for C/S (p=0.982).

Next, we studied the frequency of detection of allelic variants and polymorphism of the IL2 gene genotype association (T 330G) in patients with AD and its clinical variants with concomitant allergic diseases (AR and BA) (Table 3).

Table 3 Frequency of alleles and genotypes of polymorphism rs2069762 (T 330G) of IL 2 gene in groups of patients with atopy and controls

№	Group	Frequency of alleles				Frequency of alleles					
		T		G		T/T		T/G		G/G	
		n	%	n	%	n	%	n	%	n	%
1	Basic group n=100	122	61,00	78	39,00	41	41,00	40	40,00	19	19,00
1.1	Atopic dermatitis n=53	60	56,60	46	43,40	17	32,08	26	49,06	10	18,87
1.2	Atopic dermatitis + allergic rhinitis n=30	36	60,00	24	40,00	14	46,67	8	26,67	8	26,67
1.3	Atopic dermatitis + bronchial asthma n=17	26	76,47	8	23,53	10	58,82	6	35,29	1	5,88
2	The control group n=98	136	69,39	60	30,61	54	55,10	28	28,57	16	16,33

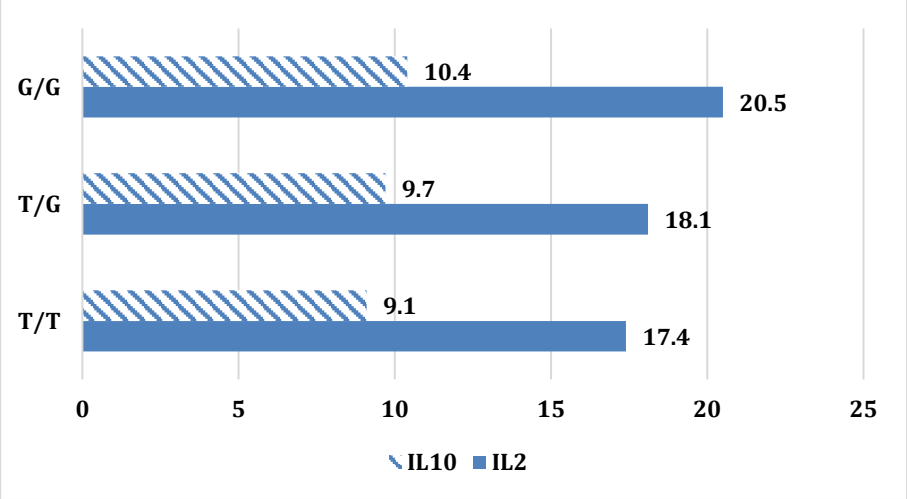
Our study of the frequency of distribution of alleles of the rs2069762 (T330G) polymorphism of the IL2 gene in a sample of patients in the main group and in the population sample (control) showed that the mutant "G" allele was more common in patients with atopy than in the control (39.0% and 30.6%, respectively; $\chi2=3.07$; $p<0.1$; OR=1.45; 95%CI 0.957-2.195), while the frequency of the "wild" allele "T" was higher in the control group (61.0% – the main group; 69.4% – the control group; $\chi2=3.07$; $p<0.1$; OR=0.69; 95%CI1.045-0.456). The data obtained in our study indicate a weak association between the "G" allele of the rs2069762 (T330G) polymorphism of the IL2 gene and atopic pathology, the chance of which increases by 1.45 times in the presence of this genetic determinant (OR=1.45) (Table 3).

In the subgroups of patients, only sAD(1.1) and with AD+AR (1.2) the variant allele "G" was also more common than in the population control group (control: 30.6%; BP: 43.4% - $\chi2=4.94$; $p<0.05$; OR=1.74; 95%CI 1.067-2.830; BP+AP: 40.0% - $\chi2=1.84$; $p<0.2$; OR=1.51; 95%CI 0.832-6.0), while only the difference in the frequency of the mutant allele in the sample of patients with BP alone was significant. In the subgroup of patients whose BP was complicated by bronchial asthma (subgroup 1.3), the frequency of the "G" allele, on the contrary, was lower than in the control group (control: 30.6%; BP+BA: 23.5% -2=0.70; $p<0.5$; OR=0.70; 95%CI 1.624-0.299), however, the lack of statistical confirmation of this difference with the control does not allow us to associate the low frequency of the variant allele with the pathogenesis of AD associated with asthma.

Thus, the data of our study showed the presence of an associative relationship between the heterozygous T/G genotype of the rs2069762 (T330G) polymorphism of the IL2 gene and the development of blood pressure, increasing the risk of pathology by 2.4 times. However, the presence of this genotype in the genome of AD patients paradoxically prevents them from developing allergic rhinitis in the future, reducing the risk of its occurrence by 2.6 times. The data obtained indicate the association and ambiguity of the effect on the pathogenesis of atopy of the T/G genotype, which contributes to the development of blood pressure and has a protective effect against the development of allergic rhinitis.

In the course of the study, we analyzed the state of pro-(IL-2) and anti-inflammatory (IL-10) cytokines and total IgE, taking into account allelic variants of the rs2069762 (T330G) IL2b gene in a group of AD patients with dermatorespiratory syndrome. Thus, in patients with heterozygous and homozygous variants of the unfavorable T/G and G/G allelic variants, the level of total immunoglobulin E was 1.05 and 1.3 times higher than in patients with favorable T/T(T330G) genotypes of the IL2 gene. The results obtained were statistically significant. ($P<0.05$)

Drawing 1: Indicators of pro-(IL-2) and anti-inflammatory (IL-10) cytokines in patients with hypertension, taking into account the polymorphism of the rs2069762 (T330G) IL2 gene variants (pg/ml).



In studies of the proinflammatory cytokine IL-2, taking into account the allelic variants of the (T330G) IL2 gene, an increase of 1.04 and 1.2 times was revealed in patients with unfavorable genotypes of the (T330G) IL2 gene compared with the functional genotypes of the T/T IL2 gene, which was statistically significant. ($P < 0.05$)

Thus, the results of the studies published in the literature and our own research indicate that the proinflammatory cytokine IL-2 plays an important role in the development of atopic pathology. The action of IL-2, realized through the IL-2R receptor on the surface of T-helper cells, leads to activation of signaling and the development of inflammatory and immune reactions. The data obtained dictates the development of new approaches to pathogenetic therapy in patients with hypertension

REFERENCES

[1] Saeki, H., Ohya, Y., Arakawa, H., Ichiyama, S., Katsunuma, T., Katoh, N., ... & Furuta, J. (2025). Executive summary: Japanese guidelines for atopic dermatitis (ADGL) 2024. *Allergology International*.

[2] Davis, D. M., Drucker, A. M., Alikhan, A., Bercovitch, L., Cohen, D. E., Darr, J. M., ... & Sidbury, R. (2022). American Academy of Dermatology Guidelines: awareness of comorbidities associated with atopic dermatitis in adults. *Journal of the American Academy of Dermatology*, *86*(6), 1335-1336.

[3] Wang, Q., Liu, L., Gao, S., & Su, S. (2023). Guidelines for the management of atopic dermatitis in children: a systematic review. *International Archives of Allergy and Immunology*, *184*(2), 132-141.

[4] Arents, B. W., van Zuuren, E. J., Vermeulen, S., Schoones, J. W., & Fedorowicz, Z. (2022). Global Guidelines in Dermatology Mapping Project (GUIDEMAP), a systematic review of atopic dermatitis clinical practice guidelines: are they clear, unbiased, trustworthy and evidence based (CUTE)?. *British Journal of Dermatology*, *186*(5), 792-802.

[5] Zakirovna, M. S., Maksudovich, E. M., Rustamovna, I. G., & Khamdamovich, Z. B. (2022). The Role Of The Filaggrin Gene In The Mechanism Of The Formation Of Atopic Dermatitis In Children Of The Uzbek Population. *Journal of Pharmaceutical Negative Results*, *13*.

[6] Zhanabaeva, G. U., Ismailova, Z. A., & Muldabekova, K. A. (2025). Immunoglobulin E and its significance in chronic dermatoses (psoriasis and vitiligo). *Russian Journal of Immunology*, *28*(2), 195-200.

[7] LePoidevin, L. M., Lee, D. E., & Shi, V. Y. (2019). A comparison of international management guidelines for atopic dermatitis. *Pediatric dermatology*, *36*(1), 36-65.

[8] Kulthanan, K., Tuchinda, P., Nitiyarom, R., Chunharas, A., Chantaphakul, H., Aunhachoke, K., ... & Noppakun, N. (2021). Clinical practice guidelines for the diagnosis and management of atopic dermatitis. *Asian Pacific journal of allergy and immunology*, *39*(3), 145-155