



**SIGNIFICANCE OF G197A POLYMORPHISM OF THE IL-17 A GENE DEPENDING ON
THE COURSE OF REACTIVE ARTHRITIS**

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Annotation:

In patients with reactive arthritis (ReA), cytokines produced by Th17 cells, one of them IL-17, affect cell differentiation, recruitment, activation of immune cells, and release of antimicrobial peptides. Among the cytokines of the IL-17 family, it is IL-17A that is of decisive importance in the induction of pathological bone resorption through direct activation of osteoclast precursors during the formation of the articular syndrome. The aim of our work was to study the distribution of allele and genotype frequencies of the polymorphic region G197A (rs2275913) of the IL-17A gene in patients with ReA. As a result of the study, there were no significant differences in the distribution of alleles of the G197A polymorphism of the IL-17A gene in patients with ReA and apparently healthy people. But when comparing genotypic variants, we revealed differences: healthy GG and mutant AA genotypes were more common in patients, while the heterozygous GA genotype was more common in healthy people.

Keywords: reactive arthritis, cytokines, polymorphism, IL-17A, genotype

Reactive arthritis (ReA) is an inflammatory non-suppurative joint diseases that develop in close chronological order connection with past intestinal or urogenital infection. They belong to the group of seronegative spondyloarthritis (SpA) and are usually associated with the presence of the HLAB27 antigen. In recent years, the pathogenetic role of cellular toll-like receptors activated by chlamydia ligands has been actively discussed, as well as the hypothesis of cytokine imbalance, the ineffectiveness of the immune response, which consists in insufficient elimination of pathogens and their antigens from the joint cavity. The results of numerous studies indicate that ReA immunopathogenesis is a complex multicomponent process of interaction between cellular and humoral components of immunity, with T-lymphocytes and an imbalance of pro-inflammatory and anti-inflammatory cytokines playing a key role.

According to the literature, patients with ReA are considered as Th17/Th1-dependent autoimmune diseases. Cytokines produced by Th17 cells, one of them IL-17, affect cell differentiation, recruitment, activation of immune cells, and release of antimicrobial peptides. Among the cytokines of the IL-17 family, it is IL-17A that is of decisive importance in inducing pathological bone resorption through direct activation of osteoclast precursors during the formation of the articular syndrome.

In articular syndrome, IL-17 stimulates the synthesis of effector molecules capable of activating various target cells, such as osteoclasts, B-lymphocytes and macrophages, responsible for the arthropathy-



specific inflammatory response and bone remodeling. The gene encoding the production of IL-17A is located on chromosome 6p12. As a result of the 1000 Genomes project (<http://www.1000genomes.org>), data have been obtained on a number of single nucleotide polymorphisms (SNPs) in the genes of the IL-17 family, including those in the promoter, exons, and intron regions. Some polymorphisms are known in the promoter and coding regions of IL17 genes associated with the level of IL-17 concentration in blood serum.

Purpose: to study the distribution of allele and genotype frequencies of the polymorphic region G197A (rs2275913) of the IL-17A gene in patients with ReA.

Materials and methods: The study was conducted in the third city clinical hospital in the department of rheumatology. The study was conducted in 86 patients (53 women, 33 men, 20-50 years old) with ReA. The control group consisted of 24 practically healthy volunteers, without burdened rheumatological anamnesis (Table №1).

Table №1 Characteristics of patients with ReA

Indicators	Characteristics, n=86
Women/men	53/33
Average age (in years)	35,5±15
Duration of illness (in years)	4,5±3,1
Disease activity according to DAS28	>5,1
ESR	35,2±4,1

ReA was diagnosed according to the American College of Rheumatology (ACR) criteria and disease activity was calculated using the DAS 28 calculator.

Static processing of the data obtained during the study was carried out using the computer program EXCEL and STATISTICA 6.0. To identify the correspondence of genotype distributions to the expected values at Hardy-Weinberg equilibrium and to compare the distributions of genotype and allele frequencies in two subpopulations, the χ^2 test (Pearson) was used, where $p < 0.05$ was considered statistically significant. The limits of the 95% confidence interval (CI) were calculated by the method of B. Woolf.

Genomic DNA was extracted from whole blood collected in EDTA tubes using the GeneMATRIX Quick Blood DNA Purification Kit (Poland). Identification of all studied polymorphisms in the IL17A gene was performed using the TaqMannSNP genotyping test: 17A (IL-17A G-197A). The reaction was carried out in duplicate using the Fast Real-Time PCR Detection System (Germany).

Results and Discussion

In our study, 86 patients with ReA and 24 healthy volunteers without a rheumatological history were studied. All patients underwent genotyping of the G197A polymorphism of the IL-17A gene.



According to the results of genotyping, all patients were divided into three groups: the first group was patients with a healthy GG genotype, the second group was patients with a heterozygous GA genotype, and the third group was a carrier of a mutant AA genotype.

As can be seen from Table №2, the first group with a healthy GG genotype of the IL-17A gene occurred in 34.2% of patients, while in the control group it occurred in 22.6% of cases, and significant differences were found between patients with ReA and the control group (OR = 0.7124; 95% CI: 0.358 > 0.482 > 0.846; $\chi^2 = 8.417$ (p=0.005113)).

Table №2 Distribution of genotypes of the G197A (rs2275913) polymorphism of the IL-17A gene

Genotypes of the G197A polymorphism of the IL-17A gene	GG (%)	GA (%)	AA (%)
Patients with ReA n=86	34,2	48,2	28,2
Control group	22,6	32,1	17,7
χ^2	8.417	2,347	5.489

In the second group, whose representatives were heterozygous patients, the GA genotype was found in 48.2% of patients, in the control group it was significantly higher and amounted to 32.1% of cases (OR = 1.261; 95% CI: 0.723 > 1.417 > 3.627; $\chi^2 = 2.347$), however, they did not reach true significance. The frequency of occurrence of the mutant AA genotype (third group) was 28.2% and in the control group 17.7%. (Table №2) and a risk marker for the development of ReA was the A allele and the homozygous AA genotype (OR = 5.647; 95% CI: 0.8247 > 5.256 > 32.781; $\chi^2 = 5.489$ (p = 0.04781)).

Table №3 Allele distribution of the G197A polymorphism of the IL-17A gene

Allele	n	%
Patients with ReA		
G	45	52,5
A	12	46,2
Control group		
G	13	51,1
A	11	48,3

As can be seen from Table №3, the percentage of the G and A alleles were almost the same in healthy and sick people. The G allele of the G197A isoform was found in 52.5% of patients and in 51.0% of healthy individuals. The A allele was found in 46.2% of ReA patients and in 48% of healthy controls. Conclusions: Thus, there were no significant differences in the distribution of alleles of the G197A polymorphism of the IL-17A gene in patients with ReA and healthy controls. But when comparing



genotypic variants, we revealed differences: healthy GG and mutant AA genotypes were more common in patients, while the heterozygous GA genotype was more common in healthy people. The data obtained, in general, indicate that in patients with ReA the frequency of the allelic variant G IL17A (rs2275913) is significantly higher, which may indicate its certain role in the development of articular pathology.

References

1. Abdurakhmanova N., Akhmedov K. AB0001 ASSOCIATION OF MDR1 GENE G2677T POLYMORPHISM WITH METHOTREXATE RESISTANCE IN PATIENTS WITH UZBEK RHEUMATOID ARTHRITIS. – 2019.
2. Ibtissam Bentaleb, Kawther Ben Abdelghani, Samira Rostom, Bouchra Amine, Ahmed Laatar,² and Rachid Bahiri¹ Reactive Arthritis: Update Curr Clin Microbiol Reports. 2020, 26.09: 1–9. doi: 10.1007/s40588-020-00152-6.
3. Khalmetova F. I. et al. Immunological Features of Reactive Arthritis of Various Etiologies // Journal of Coastal Life Medicine. – 2023. – T. 11. – С. 1322-1325.
4. Бекенова Н. Б., Гржибовский А. М., Муковозова Л. А., Смаил Е. М., Токаева А. З. Полиморфизм rs8193036 гена ИЛ-17А в казахской популяции и его связь с продукцией ИЛ-17А у больных рожей // Экология человека. 2016. №4.
5. Бочкарева Л.С., Миromanова Н.А., Миromanов А.М. Роль полиморфизма генов некоторых молекул иммунного ответа в развитии острого вирус-индуцированного бронхиолита. Журнал инфектологии. 2022;14(4):77-87. <https://doi.org/10.22625/2072-6732-2022-14-4-77-87>
6. Смольникова Марина Викторовна, Барило Анна Александровна, Смирнова Светлана Витальевна Полиморфизм генов цитокинов (IL7a и IL17F) при псориазе и псориатическом артрите // Сибирское медицинское обозрение. 2018. №5 (113).