MOLECULAR GENETIC DIAGNOSTICS FOR ULCERATIVE COLITIS

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Abstract: Over the past two decades, increasing attention has been paid to the development and implementation of molecular genetic technologies for diagnosing and predicting the risk of developing and progressing inflammatory bowel diseases (IBD). Cytokine gene expression begins in response to antigenic stimulation or tissue damage. In UC, increased production of cytokines is observed: interleukin 1β (IL 1β), IL 5, IL 6, IL 8, IL 13, IL 17, IL 22, tumor necrosis factor α (TNFα), andTL1A.

Keywords: CARD15 gene, polymorphism, genetic testing, ulcerative colitis, interleukins.

Introduction

The 21st century has seen a steady increase in the prevalence of inflammatory bowel diseases, particularly in economically developed countries and among young working-age individuals. Despite significant advances in gastroenterology, the pathogenesis of ulcerative colitis and Crohn's disease, as well as the potential for early diagnosis and prognosis of their clinical course, remain unresolved. The lack of clear prognostic criteria complicates the timely administration of pathogenetically based therapy and can contribute to disease progression and a decrease in patients' quality of life. Traditional diagnostic methods—clinical, endoscopic, morphological, and radiological—allow for an objective assessment of the location, extent, and activity of the inflammatory process. However, their information content is most valuable once the clinical and morphological picture has matured. The ability

to detect the disease early and predict its course using these methods remains limited. The development of molecular genetics and decoding of the human genome contributed to the formation of a new direction in the study of inflammatory bowel diseases. Currently, a significant number of single nucleotide polymorphisms have been identified that are associated with various parts of the pathogenesis of ulcerative colitis and Crohn's disease. Among them, the genes CARD15 (NOD2), TLR2, TLR4, TLR9, TNF-α, IL-10, IL-23R, STAT3, JAK2, ATG16L1, IRGM and a number of others are of particular interest. Their influence on the formation of genetic predisposition, clinical phenotype of the disease and response to therapy is being studied. The NOD2 gene (CARD15), located on chromosome 16q12, is involved in the regulation of the innate immune response, ensuring the recognition of bacterial components and the activation of nuclear transcription factors that control the synthesis of proinflammatory cytokines. The most studied variants are Arg702Trp, Gly908Arg, and Leu3020insC, which in some populations are associated primarily with Crohn's disease. However, the severity and nature of genetic associations vary depending on ethnicity and geographic region. The TNF-α gene, encoding one of the key proinflammatory cytokines, plays a significant role in the pathogenesis of ulcerative colitis. The polymorphic variants -308G/A and -238G/A have different effects on gene expression: the presence of the A allele at position -308 is accompanied by increased transcriptional activity, while a substitution at position -238 can lead to decreased TNF-α synthesis. Some studies indicate a possible association between the -308G/A variant and the age of disease onset, the severity of its course, and the frequency of relapses. Despite the accumulated data, the use of genetic markers in routine clinical practice remains controversial. International professional societies point to the need for further population-based studies that take into account ethnic characteristics and the multifactorial nature of the disease. The immunopathogenesis of ulcerative colitis involves T-lymphocytes, antibodies, the complement system, reactive oxygen

species, proteolytic enzymes, and apoptotic mechanisms. Cytokines, interferon-γ, growth factors, adhesion molecules, and intracellular signaling pathways play a significant role. Genetic networks involved in disease predisposition are currently being actively analyzed to identify key and modifying genes. Thus, molecular genetic studies expand our understanding of the pathogenesis of ulcerative colitis and create the preconditions for the development of personalized diagnostic and therapeutic approaches. At the same time, further comprehensive studies, taking into account population differences, are needed to integrate genetic testing into clinical practice.

Conclusion. Molecular genetic studies significantly expand our current understanding of the pathogenetic mechanisms of ulcerative colitis and allow us to view the disease as a complex multifactorial process with a strong genetic component. Identifying gene polymorphisms involved in regulating the immune response and the production of proinflammatory cytokines opens the door to more precise patient stratification based on risk, clinical course, and likelihood of complications.

However, the heterogeneity of the data obtained across different populations indicates the need for further multicenter studies, taking into account ethnic and regional characteristics. Currently, molecular genetic testing should be considered as an additional tool in comprehensive diagnostics that can improve the accuracy of prognostic assessments, but does not replace traditional clinical and instrumental methods. A promising direction is the integration of genetic markers into the personalized medicine system, which will optimize the choice of therapeutic tactics and increase the effectiveness of treatment for patients with ulcerative colitis.

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