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Research Article

ROLE OF THE GENE FOR XENOBIOTICS BIOTRANSFORMATION ENZYME IN TUMOR PROGRESSION IN ACUTE LEUKEMIA

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ABSTRACT

Biotransformation enzyme genes play an important role in metabolism and processing of foreign substances (xenobiotics) in the body. Their role in tumor progression is their ability to modulate metabolic pathways by affecting the processing of xenobiotics, which may affect the development of tumors. This is a current topic of research in the field of oncology.

KEYWORDS

acute leukemia, chronic leukemia, molecular genetics, gene, polymorphism, heterozygosity, wild allele, minor allele, MDR1, rs1045642.

INTRODUCTION

The MDR1 gene encodes a protein called P-glycoprotein (P-gp), which is a member of the ATP-binding cassette (ABC) transporter family. P-gp plays a critical role in cellular drug efflux, actively pumping various drugs and toxins out of cells, thereby promoting drug resistance in cancer treatment. The

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C3435T polymorphism in the MDR1 gene involves a substitution of cytosine (C) for thymine (T) at position 3435 of the sequence and is associated with changes in P-gp expression and function, potentially affecting its ability to efficiently pump drugs out of cells. Variations in P-gp expression or function due to the C3435T polymorphism could potentially influence the metabolism of endogenous substrates or environmental toxins, which could influence cellular processes associated with leukemogenesis. Moreover, altered P-gp expression or function due to the C3435T polymorphism may disrupt cellular homeostasis, potentially leading to increased genomic instability or disruption of DNA repair mechanisms, which are known to contribute to the development of leukemia [1,2,3,4, 5].

PURPOSE OF THE STUDY

To develop a PCR method to detect the C3435T polymorphism of the MDR1 gene and evaluate its role in the formation of acute and chronic leukemia.

MATERIALS AND METHODS OF RESEARCH

The study included 103 patients suffering from acute leukemia, who were registered at the Republican Specialized Scientific and Practical Medical Center for Hematology of the Ministry of Health of the Republic of Uzbekistan, and 90 conditionally healthy individuals were selected as a control group, of which 50 people did not have oncohematological diseases or history of thrombosis.

RESULTS

Carriers of the C allele showed a significant decrease in the likelihood of developing the disease by 41% (OR = 0.59, 95% CI: 0.39-0.89; p = 0.01), while the minor T allele of the MDR1 C3435T gene significantly increased the risk 1.69 times (OR = 1.69; 95% CI: 1.13-2.55; p = 0.01). Analysis of the C3435T polymorphism showed that the TT genotype increases the risk of the disease by 2.31 times (OR = 2.31; 95% CI: 1.09-4.89; p = 0.027), while the CC genotype demonstrates a 44% reduction in risk (OR = 0.56, 95% CI: 0.31-1.03, p = 0.06). It is noteworthy that in this study, the TT genotype was found to be a significant risk factor for the development of the disease.

In our study, the main group of patients (n=103) was divided into subgroups depending on the acute (first subgroup) or chronic (second subgroup) course of leukemia. Regarding the pathogenetic significance of the C3435T polymorphism of the MDR1 gene in the first subgroup, carriers of the C allele had a noticeable reduction in the likelihood of developing the disease by 48% (OR = 0.52, 95% CI: 0.32-0.84; p = 0.008). Conversely, the minor T allele of the MDR1 C3435T polymorphism significantly increased the risk of the disease by 1.93 times (OR = 1.93; 95% CI: 1.19-3.15; p = 0.008), becoming a significant risk factor for the development of acute leukemia in our research. On the other hand, our study did not reveal a statistically significant relationship between the second group (chronic leukemia) and the C3435T polymorphism of the MDR1 gene ($\chi 2 < 3.85$; $p > 0.05$).

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CONCLUSION

In our study, the minor allele (T) of the C3435T polymorphism of the MDR1 gene demonstrated a significant positive association with acute leukemia (OR=1.93; 95% CI: 1.19-3.15, $\chi 2=7.13$; $p=0.008$). On the contrary, no statistically significant relationship was observed between the second group (chronic leukemia) and the C3435T polymorphism of the MDR1 gene ($\chi 2<3.85$; $p>0.05$).

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