

Summary

Changes in the function of transport proteins can lead to disorders of cellular homeostasis, loss of protective mechanisms in the cell by slowing down or inhibiting the elimination of harmful substances from the cell, which may result in their accumulation in the cell. This may significantly increase the risk of damage and mutations leading to the development of cancer. Genetic variants such as SNPs resulting in changes in protein structure, activity or changes in expression of genes encoding transport proteins may affect the risk of cancer development. On the other hand, SNPs within the genes encoding transport proteins may affect the effectiveness of anticancer therapy by modifying the effective transport of chemotherapeutic agents, the cellular response to chemotherapy, or by inducing the mechanism of multidrug resistance.

Taking into account the above premises, the aim of the doctoral dissertation was to assess the role of polymorphisms of genes encoding selected cellular transporters from the ABC superfamily and the OATP family in the predisposition of multiple myeloma development and effectiveness of anticancer therapy. Individual SNPs were selected on the basis of data available in the literature and with the use of on-line genetic databases (COSMIC, NCBI). In the research carried out as part of the doctoral dissertation, four polymorphisms within three selected genes encoding transport proteins from the ABC and OATP families were assessed. Using the PCR-RFLP technique, the following gene polymorphisms were assessed: ABCB1 (rs3213619), ABCG2 (rs2231137, rs2231142) and SLCO1B1 (rs2306283). The study involved 181 patients diagnosed with multiple myeloma treated at the Hematology Department of the Medical University of Lodz in the years 1992-2002. The tested material was DNA isolated from peripheral blood collected on EDTA. In addition, 141 samples of DNA isolated from healthy individuals were used as a reference group.

The research carried out and the analysis of the obtained results allowed for the formulation of preliminary conclusions. A statistically significant association was found between the occurrence of the SNP C421A polymorphism (rs2231142) of the ABCG2 gene and an increased risk of developing multiple myeloma, as well as the association between the presence of the A388G polymorphism (rs2306283) of the SLCO1B1 gene and age in the groups below and above 63 years of age. In addition, the association of this polymorphism with the overall survival of patients was demonstrated, showing that the GG genotype of the A388G polymorphism of the SLCO1B1 gene is associated with longer survival when using the MP regimen in relation to other analyzed types of therapy in multiple myeloma.

In the remaining cases, there were no statistically significant differences in the frequency of individual genotypes and alleles of the tested SNPs between the study group and the control group, as well as age, sex, available clinical data, type of therapy scheme and survival of patients with multiple myeloma. They probably have no connection with the development, course and effectiveness of multiple myeloma treatment. However, further studies are needed to obtain more comprehensive genetic profiles of membrane transporters and their differential regulation in cancer cells.