**MDR1 (ABCB1)** gene polymorphism C3435T is associated with P-glycoprotein activity in B-cell chronic lymphocytic leukemia

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**Abstract:**

Functional single nucleotide polymorphism (SNP) C3435T in exon 26 of the MDR1 (ABCB1) gene encoding the xenobiotic transporter P-glycoprotein (P-gp, MDR1, ABCB1) may influence susceptibility to several diseases as well as clinical outcome of treatment with P-gp substrates. Exposure to environmental chemicals is thought to be involved in the pathogenesis of B-cell chronic lymphocytic leukemia (B-CLL) and P-gp-transported drugs are used in its treatment; however, little is known about the impact of the C3435T MDR1 SNP in B-CLL. In this study, 110 Caucasian B-CLL patients and 201 healthy controls were genotyped for the MDR1 C3435T SNP. Additionally, P-gp activity was assessed in malignant lymphocytes of 22 untreated B-CLL patients. We observed a higher frequency of carriers of at least one 3435T allele (3435CT and 3435TT genotypes) among B-CLL patients as compared to normal individuals (76% vs. 63%, p = 0.027). The genotypes 3435CT and 3435TT were associated with B-CLL, (odds ratio = 1.8, 95% confidence interval = 1.1–3.0). Moreover, P-gp activity in B-CLL cells depended on MDR1 genotype, with the highest P-gp activity in 3435CC homozygotes, intermediate in 3435CT heterozygotes and the lowest in 3435TT homozygotes (p = 0.042). P-gp activity was also significantly lower in carriers of the T-allele (3435CT/TT genotype) as compared to the non-carriers (3435CC genotype), (p = 0.029). Taken together, these data indicate that the MDR1/C3435T SNP may carry an increased risk of developing B-CLL, possibly by virtue of decreased protection against P-gp-substrate carcinogens. The differences in P-gp activity in B-CLL tumor cells related to MDR1 genotype may have implications to the response to chemotherapy with P-gp transported anticancer agents.

**Key words:**

B-CLL, genetic susceptibility, MDR1, ABCB1, polymorphism, multidrug resistance