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Association of *MDR1* gene C3435T (rs1045642) polymorphism with colorectal cancer in the population of Central Russia

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Motivation and Aim: Colorectal cancer (CRC) is one of the most common cancers worldwide. Currently, the incidence of CRC tends to increase. Genetic factors together with environmental factors might increase the risk of colorectal cancer [1]. It is well known that genes encoding drugs metabolism enzymes are involved in the pathogenesis of colorectal cancer. The multidrug resistance gene 1 (MDR1, ATP binding cassette subfamily B member 1, ABCB1) encodes a transmembrane glycoprotein P, involved in the transformation of drugs. Recent studies indicated MDR1 gene seemed to play an important role in tumor progression, especially in the colorectal carcinogenesis [2].
Methods and Algorithms: A total 379 unrelated Russian subjects including 244 CRC patients and 135 age- and sex-matched controls were recruited for this study. Genomic DNA was isolated from peripheral blood samples using a standard phenol/chloroform procedure. Genotyping of the 3435C>T polymorphism (rs1045642) of the *MDR1* gene was done using TaqMan-based assay on the CFX96 real-time PCR Detection System. Hardy-Weinberg equilibrium was tested to compare the observed and expected genotype frequencies among cases and controls using chi-square test. The association between the polymorphism and CRC risk was estimated by odds ratio (OR) with 95 % confidence interval (CI). The statistical significance was established at $P<0,05$. Statistical calculations were performed with Statistica for Windows 8.0.
Results: The MDR1 genotype frequencies were in agreement with Hardy-Weinberg equilibrium in CRC and control groups ($P >0,05$), which indicates uniformity of the sample. The frequency of homozygous genotype 3435CC was 22,1 % in patients and 33,3 % in healthy controls. The frequency of heterozygous genotype 3435CT was 50,4 and 47,4 % in patients and controls, respectively. Homozygous genotype 3435TT was observed in 27,5 % of cancer patients and in 19,3 % of healthy individuals. Thus, we have established that homozygous genotype 3435CC of the *MDR1* was associated with protective effect against the risk of CRC (OR = 0,57; 95%CI = 0,36–0,91; P = 0,02).
Conclusion: In conclusion, our study showed that MDR1 C3435T polymorphism might be significantly associated with risk of CRC in the population of Central Russia. Further studies, especially the gene–gene and gene–environment interactions are required.

References

1. Grady W.M., Carethers J.M. (2008). Genomic and epigenetic instability in colorectal cancer pathogenesis. Gastroenterol. 135(4):1079-1099.
2. Chin J.E., Soffir R.E.N.A., Noonan K.E., Choi K. Y. U. N. G. H. E. E., Roninson I.B. (1989). Structure and expression of the human MDR (P-glycoprotein) gene family. Mol. Cell. Biol. 9(9):3808-3820.