**IMPACT OF APEX ILE64VAL GENE POLYMORPHISMS OF DNA REPAIR BER SYSTEM ON MODULATION OF THE RISK OF COLORECTAL CANCER IN THE POLISH POPULATION**

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Colorectal cancer (CRC) is one of the deadliest cancers which lie in the incidence of morbidity in second place. Intensive research is to determine and confirm the genetic basis of this disease, which is believed may have a direct relationship with the reduced efficiency of DNA repair systems.

The aim of this study was to determine the effect of APEX gene polymorphism Ile64Val on increasing the risk of colorectal cancer in the Polish population.

**Material and methods.** The blood samples collected from 150 patients diagnosed with colon cancer was used. The control group consisted of 150 healthy subjects. Genotyping was performed by TaqMan method.

**Results.** The results indicate that genotype Ile Val is associated with an increased risk of colorectal cancer (OR 2.069; 95% CI 1.205-3.552; p = 0.008).

**Conclusions.** Based on these results, we conclude that the APEX gene polymorphism Ile64Val may be associated with an increased risk of colorectal cancer.

**Keywords:** colorectal cancer, polymorphisms, APEX, DNA repair

Base excision repair (BER) is a DNA repair mechanism that occurs in human cells. It eliminates damage to a single nitrogen bases which are formed by chemical modification such as oxidation, deamination or alkylation. Such damage, if not repaired, can lead to mutations through incorrect pairing and strand breaks during DNA replication. The fixation of the resulting mutations may lie at the basis of the process of carcinogenesis. Amount of mutations occurring in cells is directly proportional to the effectiveness of DNA repair systems, which translates into a greater risk of cancer in the case of a reduced level of damage repair. This has been confirmed in the case of Lynch syndrome (Hereditary non-polyposis colorectal cancer, HNPCC), whose aetiology is derived from mutations in MMR repair system (1, 2).

APEX1 gene encodes an enzyme AP lyase (DNA apirymidine or apurine lyase), which plays a crucial role in the repair of DNA damage. AP sites arise as a result of spontaneous hydrolysis or oxidative damage or as a result of glycosylase activity, which are a component of the BER repair system and remove the damaged bases and creating an apurine/apirymidine site. Nucleosides lacking nitrogen base are highly mutagenic and in that case it is practically impossible to perform correct DNA replication. AP lyase begins the process of repair of the AP site as part of the BER pathway maintaining the stability of the genome of the cell. Both

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for this reason and due to its interaction with proteins MUTYH (3) and XRCC1 (4) which are the key components which affect the efficiency of DNA repair it should be suspect that APEX gene polymorphisms may affect the level of repair activity in the BER pathway and therefore modulate the risk of carcinogenesis.

The aim of this study was to determine the effect of APEX gene polymorphism Ile64Val on the risk of colorectal cancer in the Polish population.

MATERIAL AND METHODS

Experimental material

Test DNA was isolated from peripheral blood samples collected from 150 unrelated patients. All patients had histologically confirmed colorectal cancer. The study group consisted of 78 men and 72 women (mean age 61 ± 8). To assess the stage of cancer TNM scale was used. A detailed information about the patients illustrates tab. 1. The control group consisted of 150 persons age corresponding to the study group who did not have cancer.

Methods

DNA isolation was performed with commercial kit QIAamp DNA Blood Mini Kit for isolation of high-molecular-weight DNA (Qiagen). The distribution of polymorphic variants APEX Ile64Val was examined using TaqMan method. Test polymorphism refSNP is 2307486.

Statistical analysis

The resulting number of each genotype was compared with the expected value based on Hardy–Weinberg equilibrium. The significance of differences between the frequencies of alleles and genotypes between groups was assessed using χ² test. The risk of an event was assessed using multivariate regression analysis (odds ratio, OR) with corresponding confidence interval 95% (CI 95%).

RESULTS

Table 2 presents the analysis of the distribution of polymorphic variants of the gene APEX Ile64Val and their correlation with the modulation of the risk of colon cancer. Studies indicate that genotype Ile/Val may affect the increased risk of CRC (OR 2.069; 95% CI 1.205-3.552; p = 0.008).

DISCUSSION

Determination of the effects of polymorphisms of DNA repair genes on process of carcinogenesis will allow certain polymorphisms to be associated with increased risk of cancer, and thus the eligibility of patients to high-risk groups. This is already the case with the aforementioned HNPCC and gene polymorphisms in the MMR system, but this is only one type of colorectal cancer, and further studies are required to reconcile different types of polymorphisms of BER or NER systems with CRC. Particularly in the case of sporadic cancer finding such a correlation appears to be extremely important, because it would be a very useful diagnostic tool for patients who do not exhibit any other suitability for CRC. Ongoing research suggests a number of possible relationship of polymorphisms of genes in BER system such as XRCC1 (5, 6) and OGG1 (7, 8).

Given the previously described function of APEX in BER mechanism it is also suspected to have the potential contribution in the pathogenesis of CRC. So far conducted studies on APEX Ile64Val gene polymorphisms focused on confirming the role in the modulation of...
Impact of APEX ile64val gene polymorphisms and the risk of colorectal cancer

In the field of colorectal cancer previous reports do not specify explicitly the effect of the increased risk of CRC (12). Our results suggest that genotype Ile/Val is associated with an increased risk of colorectal cancer (OR 2.069; 95% CI 1.205-3.552; p = 0.008). However, given the complexity of the process of carcinogenesis, and the important role of intergenic interactions further studies to determine the undeniable link between APEX and the increased risk of CRC are necessary. Especially in view of the use of the results of both the eligibility of patients for increased risk groups, as well as in later stages to predict response to anti-cancer treatment, depending on the prevalence of polymorphisms data (13, 14).

**CONCLUSION**

Based on these results, we conclude that the APEX gene polymorphism ile64Val may be associated with an increased risk of colorectal cancer.

**REFERENCES**


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