GENETIC POLYMORPHISMS OF THREE DNA-REPAIR GENES (*PRKDC*, *XPD*, *XRCC1*) ARE RELATED TO COLORECTAL CANCER SUSCEPTIBILITY

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Although the specific causes of colorectal cancer (CRC) are not known, a robust DNA repair capacity may decrease the risk of this malignancy. DNA repair capacity may be reduced by alterations of genes involved in DNA repair process. This may affect susceptibility to carcinogenesis. It is hypothesized that single nucleotide polymorphisms (SNPs) of several DNA repair genes may be a risk factor for CRC susceptibility and prognosis. Using PCR–RFLP method, we conducted a case–control study to genotype 291 patients with CRC and 140 healthy individuals to determine variants in the PRKDC, XPD and XRCC1 genes. Results showed that the genotypes of XRCC1 c.580C>T polymorphism were associated with the risk of CRC. Compared with CC, CT (odds ratio (OR) = 5.35, P < 0.001) and CT/TT (OR = 4.74, P < 0.001) as well as T allele (OR = 4.95, P < 0.001) were overrepresented among the CRC patients. Variant genotype CC (OR = 2.37; P = 0.042) and C allele of XPD c.2251A>C (OR = 1.37; P =0.028) polymorphism, enhanced the risk of CRC cases. Compared with GG, positive association was also obtained for all genotypes (GT, TT, GT/TT) of PRKDC rs7003908; 6721G>T polymorphism with CRC. Moreover, T allele of PRKDC demonstrated significant risk for CRC (OR = 5.61; P < 0.001). Besides, significant relevance of the PRKDC rs7003908; 6721G>T variations to smoking as well as XPD c.2251A>C variations to smoking and alcohol consumption in individuals with CRC was observed. Our findings indicated that genetic polymorphisms of PRKDC, XRCC1, XPD genes may influence susceptibility of CRC in the Iranian population.

***Key words*:** *PRKDC, XPD, XRCC1, colorectal cancer, polymorphisms, cancer susceptibility.*

ГЕНЕТИЧНІ ПОЛІМОРФІЗМИ ТРЬОХ ГЕНІВ РЕПАРАЦІЇ ДНК (*PRKDC*, *XPD*, *XRCC1*) ПОВ'ЯЗАНІ ЗІ СХИЛЬНІСТЮ ДО КОЛОРЕКТАЛЬНОГО РАКУ

Хоча конкретні причини колоректального раку (CRC) залишаються невідомими, повноцінна здатність до репарації ДНК може знижувати ризик цього злоякісного захворювання. Здатність до репарації ДНК може бути знижена через зміну генів, залучених до цього процесу. Це може вплинути на схильність до онкогенезу. Існує припущення, що однонуклеотидні поліморфізми (SNPs) декількох генів репарації ДНК можуть бути фактором ризику для схильності до CRC та його прогнозування. За використання методу ПЛР-ПДРФ ми провели дослідження «випадок-контроль» з метою генотипування 291 пацієнта з CRC та 140 здорових осіб для визначення варіантів генів *PRKDC*, *XPD* та *XRCC1*. Результати продемонстрували, що генотипи поліморфізму *XRCC1* c.580C>T були пов'язані з ризиком CRC. Порівняно з CC, CT (коефіцієнт співвідношення ризиків (OR = 5,35, P < 0,001) та CT/TT (OR = 4,74, P < 0,001), а також алель T (OR = 4,95, P < 0,001) мали надмірне представлення серед пацієнтів з CRC. Варіантний генотип CC (OR = 2,37; P = 0,042) і алель C поліморфізму *XPD* c.2251A>C (OR = 1,37; P = 0,028) підвищували ризик випадків CRC. Порівняно з GG, позитивний зв'язок було також показано між всіма генотипами (GT, TT, GT/TT) поліморфізму *PRKDC* rs7003908; 6721G>T та CRC. Більше того, алель T *PRKDC* продемонстрував значний ризик щодо CRC (OR = = 5,61; P < 0,001). Крім того, спостерігалась суттєва значимість варіацій *PRKDC* rs7003908; 6721G>T щодо паління, а також варіацій *XPD* c.2251A>C щодо споживання тютюнових та алкогольних виробів особами з CRC. Наші результати демонструють, що генетичні поліморфізми генів *PRKDC*, *XRCC1*, *XPD* можуть впливати на схильність до CRC серед населення Ірану.

***Ключові слова*:** *PRKDC*, *XPD*, *XRCC1*, колоректальний рак, поліморфізми, схильність до раку.

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