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The effect of single-nucleotide polymorphism rs141831067 in Dehydrofolate reductase gene on response to methotrexate in patients with prostate cancer

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Abstract

Aim and Background: The aim of this study was to investigate the effect of rs141831067 Single nucleotide Polymorphism existence on therapeutic response of patients diagnosed with Prostate Cancer to Methotrexate and investigation of the polymorphism Frequency in Iranian population.

Material and methods: In this study, peripheral blood samples were taken from 50 healthy individuals and 50 patients suffering from prostate cancer. Then genomic DNA of each sample was extracted and isolated. ARMS-PCR and direct sequencing techniques were used to determine the presence of the polymorphism in populations. Finally, the statistical analysis of the results was performed by analyzing allelic frequency, heterozygosity, PIC analysis and Hardy Weinberg equilibrium analysis.

Results:A comparative study of rs141831067 polymorphism existence showed that the allele frequency of this marker was significantly higher in the patients relative to healthy group (P-value = 0.002). In addition the bioinformatics analyzes of the interactions of the dihydrofolate reductase enzyme and methotrexate showed that existence of the polymorphism may alter the interaction patterns and result in the relative displacement of methotrexate position from the active site of dihydrofolate reductase.

Conclusion: Rs141831067 Single nucleotide Polymorphism in Dihydrofolate reductase gene plays an important role in the prostate cancer occurrence and this Single nucleotide Polymorphism can cause drug resistance to methotrexate in prostate cancer.

Keywords: Drug resistance, Prostate cancer, Single nucleotide polymorphism, docking.

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