

# Association between single nucleotide polymorphisms in the PI3K/AKT/mTOR pathway and bladder cancer risk in a sample of Iranian population

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## Abstract

In the past few years several investigations have focused on the role of PI3K/AKT/mTOR pathway and its deregulations in different cancers. This study aimed to examine genetic polymorphisms of this pathway in bladder cancer (BC). In this case-control study, 235 patients with pathologically confirmed bladder cancer and 254 control subjects were examined. *PIK3CA*, *AKT1* and *mTOR* variants were analyzed using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP). The findings proposed that the *PIK3CA* rs6443624 SNP significantly decreased the risk of BC (OR=0.44, 95 % CI=0.30-0.65,  $p<0.0001$  CA vs CC; OR=0.35, 95 % CI=0.16-0.78,  $p=0.0107$ , AA vs CC; OR=0.60, 95 % CI=0.46-0.79,  $p=0.0002$ , A vs T). The *AKT1* rs2498801 variant is associated with a decreased risk of BC (OR=0.57, 95 % CI=0.39-0.82,  $p=0.003$ , AG vs AA; OR=0.74, 95 % CI=0.56-0.97,  $p=0.032$ , G vs A) while, *AKT1* rs1130233 polymorphism considerably increased the risk of BC (OR=3.70, 95 % CI=2.52-5.43,  $p<0.0001$ , GA vs GG; OR=5.81, 95 % CI=1.53-21.97,  $p=0.010$ , AA vs GG; OR=2.71, 95 % CI=1.98-3.70,  $p<0.0001$ , A vs G). Additionally, *mTOR* rs2295080 variant notably increased the risk of BC (OR=2.25, 95 % CI=1.50-3.38,  $p<0.0001$ , GT vs GG; OR=4.75, 95 % CI=2.80-8.06,  $p<0.0001$ , TT vs GG; OR=3.10, 95 % CI=2.34-4.10,  $p<0.0001$ , T vs G). None of the other examined polymorphisms (*AKT1* rs1130214, *AKT1* rs3730358, *mTOR* rs1883965) revealed significant association with BC. In conclusion, our findings suggest that *PIK3CA* rs6443624, *AKT1* rs2498801, *AKT1* rs1130233, as well *mTOR* rs2295080 polymorphism may be related to bladder cancer development in a sample of Iranian population. Validation of our findings in larger sample sizes of different ethnicities would provide evidence on the role of variants of PI3K/AKT/mTOR pathway in developing BC.

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