2 Estrogen receptor alpha variants as possible markers of prostate cancer development and progression

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Introduction & Objectives: Sex steroid hormones are essential in normal prostate growth, but can also serve as initiators and promoters in prostate carcinogenesis. Accumulating evidence indicates that estrogens and their corresponding receptors play crucial role in prostate cancer and might therefore represent possible markers of prostate cancer. The main aim of the study was to examine the association between single nucleotide polymorphisms located in estrogen receptor alpha gene (c.30 T/C - rs2077647, c.1029 T/C - rs3798577, PvuII T/C – rs9340799 and XbaI A/G – rs2234693) and clinical parameters of prostate cancer, such as Gleason score and age at diagnosis.

Materials & Methods: The study population consisted of 454 patients with prostate cancer and 265 healthy men. PCR-RFLP (polymerase chain reaction restriction fragment length polymorphism analysis) was used to detect selected polymorphisms. Comparison of genotype distribution and association with selected clinical data were performed with the Chi-square test and Fisher's exact test. Haplotype analysis was performed by HaploView 4.2.

Results: We found that c.30, PvuII and XbaI polymorphisms located in estrogen receptor alpha gene, but not c.1029, were significantly associated with increased risk of prostate cancer development in overall group of patients. After stratification of patients, we observed significant correlation between c.1029 and XbaI and development of high-grade carcinomas (Gleason score ≥ 7). As regard to age of patients, we detected that CGC haplotype of c.30, XbaI and PvuII polymorphisms was significantly more frequent in patients diagnosed before the age of 60 ($p = 0.009$). By analysis of different combinations of studied variants, we showed that some combinations (c.30 and PvuII, c.30 and XbaI) were associated with development of low-grade carcinomas (Gleason score ? 7), while others (c.30 and c.1029, c.1029 and PvuII, c.1029 and XbaI) were strongly associated with higher risk of development of high-grade carcinomas (Gleason score ≥ 7).

Conclusions: We can conclude that presence of estrogen receptor variants and their specific combinations could markedly contribute to higher risk of prostate cancer development as well as to early onset prostate cancer. We also found that polymorphism located in c.1029 may serve as promoting factor to development of high-grade carcinomas and after verification of this association it could be used as predictive factor of prostate cancer aggressiveness.

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