Genome-wide association study of prostate cancer

Jurečeková Jana, Babušíková Eva, Kliment Ján, Dobrota Dušan

I. INTRODUCTION

Prostate cancer is the second most frequently diagnosed malignancy and the sixth leading cause of cancer-related death in men. Prostate cancer is multifactorial disease and the major risk factors contributing to its development are age, ethnicity, environmental factors or family history of prostate cancer. Some men with prostate cancer remain asymptomatic with latent prostate carcinoma and their number is still higher than the number of men with clinically detected disease. A better understanding of the genetic and biological mechanisms that determine prostate cancer aggressiveness is needed. The genome-wide association study provides an unbiased screen for genetic loci potentially associated with prostate cancer and may help to identify new candidate genes or targets for intervention.

II. MATERIALS AND METHODS

Our study population consisted of 48 prostate cancer patients and 46 control subjects. All prostate cancer patients enrolled in this study have Gleason score ≥ 7. Blood samples, collected from all participants, were used for purification of high-quality DNA samples. The Genome-Wide Human SNP Array 6.0 was used for detection of about 900 000 single nucleotide polymorphisms. Statistical analysis of results was performed using PLINK 1.9 software package (http://pngu.mgh.harvard.edu/purcell/plink/).

III. RESULTS

We identified seven single nucleotide polymorphisms to be significantly associated with prostate cancer risk ($p < 1.0 \times 10^{-8}$) (rs12136562, rs41439745, rs9426908, rs12328643, rs9423252, rs1465512, rs2826099). Their association with prostate cancer risk remains significant ($p < 0,05$) also after Bonferroni correction for multiple testing. Three of them are located in the intergenic regions and four of them are located in genes (rs41439745 - LOC101929023, rs9426908 - PRRX1, rs12328643 - REEP1, rs9423252 - ACADSB). The exact functional impact of these polymorphisms is not known. Also direct connection between four genes, in which we detected significant polymorphisms, and prostate cancer is not described in literature. Only PRRX1 is in generally connected with the process of metastases formation, while tumors with high amounts of PRRX1 have better prognosis as they are not able to form metastases.

IV. CONCLUSIONS

Genome-wide association study represents the important tool for identification of multiple single nucleotide polymorphisms associated with susceptibility to prostate cancer, which could in the future help to predict higher risk of prostate cancer development or worse prognosis in individual patients.

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J. Jurečeková, E. Babušíková, D. Dobrota, Comenius University in Bratislava, Jessenius Faculty of Medicine in Martin, Department of Medical Biochemistry, Martin, Slovakia (e-mail: jana.jurecekova@jfmed.uniba.sk).
J. Kliment, Comenius University in Bratislava, Jessenius Faculty of Medicine in Martin and University Hospital Martin, Department of Urology, Martin, Slovakia.