Editorial

Polymorphisms and Risk of Prostate Cancer

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In the last decades, basic cancer research have provide new and fundamental insights into the combined effects of the environment and genome on individual variation in human disease risk as well into the relationship between disease susceptibility, environmental exposures and germline mutations. These efforts have showed the importance of genotype in the risk to cancer development. Genetic association studies are used to investigate natural variants or polymorphisms in the DNA sequence among individuals that might be associated with a particular disease phenotype. Variants may be single-base alterations, known as single nucleotide polymorphisms (SNPs), or they may occur as insertions or deletions of DNA fragments determining copy number polymorphisms (CNPs).

Prostate cancer is one of the most common cancers in Western countries, and a leading cause of cancer-related death. Several SNPs located on candidate genes related to the development of prostate cancer, including prostate specific antigen response component, enzymes, hormones and their receptors, cell cycle regulating protein, cytokines, adhesion molecules, vitamins and so on have been the focus of literally hundreds of epidemiologic studies. Deletions of glutathione S-transferases (GSTs) genes, especially GSTT1, are the most widely studied CNP in prostate cancer susceptibility. The evidence for a genetic susceptibility to prostate cancer has been well documented and is some of the strongest among that for all common cancers. In the context of genome-wide analyses, Amundadottir et al.[1] reported that multiple SNPs located at 8q24 had a significant association with prostate cancer susceptibility. Subsequently, in a multiple study population as well as in case control studies confirmed this region as a prostate susceptibility locus. In 2007 Gudmundsson et al.[2] reported two prostate cancer susceptibility variants located at 17q12 and 17q24.3. Interestingly, Zheng et al.[3] reported a cumulative effect of five SNPs mapped at 8q24 and 17q on prostate cancer risk in a large case-control study in Swedish individuals. They found an association between these SNPs with advanced prostate cancer.[4] However, it is no well established in the literature the relationship between these susceptibility alleles and aggressiveness in prostate cancer4. In this context, polymorphisms indicators of cancer aggressiveness are useful biomolecular markers capable of providing prognostic information to assist in the identification of the subset of patients who will benefit from aggressive treatment. Thus, a better understanding of polymorphisms, as well as the functional consequences of that variation, would provide a foundation for future studies of the possible role of individual genetic variation in the pathogenesis of prostate cancer or in response to antineoplastic drug therapy.

References

1. Amundadottir LT, Sulem P, Gudmundsson J, Helgason A, Baker A, Agnarsson BA et al. Common variant associated with prostate cancer in European and African populations. Nat Genet 2006;38:652-8.
2. Gudmundsson J, Sulem P, Manolescu A, Amundadottir LT, Gudbjartsson D, Helgason A et al. Genome-wide association study identifies a second prostate cancer susceptibility variant at 8q24. Nat Genet 2007; 39:631-7.
3. Zheng SL, Sun J, Wiklund F, Smith S, Stattin P, Li G et al. Cumulative association of five genetic variants with prostate cancer. N Engl J Med 2008;358:910-9
4. Xu J, Isaacs SD, Sun J, Li G, Wiley KE, Zhu Y et al. Association of prostate cancer risk variants with clinicopathologic characteristics of the disease. Clin Cancer Res 2008;14:5819-24.