Screening for Familial and Hereditary Prostate Cancer.


Abstract

Prostate cancer (PC) has the highest degree of genetic transmission of any form of malignancy. In some families, the hereditary pattern is so strong as to mimic an autosomal dominance trait. We reviewed the known predisposing genetic markers to assess possible strategies for screening of families at risk. We carried out a systematic literature search using the Pubmed service of the National Center for Biotechnology Information (NCBI) and several gene libraries, including the NCBI SNP Library, the Online Mendelian Inheritance in Man® Catalog of Human Genes and Genetic Disorders (OMIM) and SNPedia to obtain known gene loci, SNPs and satellite markers associated with PC. We further cross referenced information on identified loci comparing data from different articles and gene reference sites. Whenever possible, we recorded the odds ratio (OR) for the allele associated with PC. In multiple different linkage studies, many independent PC associated loci have been identified on separate chromosomes. Genome wide association studies have added many more markers to the set derived from linkage investigations. A subset of the alleles is associated with early onset and aggressive cancer. Due to the great heterogeneity, the OR for any one allele predicting future development of this malignancy is low. The strongest predictors are the BRCA2 mutations, and the highly penetrant G84E mutation in HOXB13. The presence of multiple risk alleles is more highly predictive than a single allele. Technical limitations on screening large panels of alleles are being overcome. It is appropriate to begin supplementing prostate specific antigen testing with alleles, such as BRCA2 and HOXB13, disclosed by targeted genomic analysis in families with an unfavorable family cancer history. Future population studies of PC should include genomic sequencing protocols, particularly in families with a history of PC and other malignancies. This article is protected by copyright. All rights reserved.

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