Application of SNP Interaction Pattern Identifier (SIPI) to detect gene-gene interactions in the 8q24 region associated with prostate cancer risk in African American men

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Abstract:

African American (AA) men have a higher risk to develop prostate cancer (PCa) than Whites. While the causes of PCa are not fully understood, genetic variation has a clear impact on disease. Most single nucleotide polymorphism (SNP) association studies are focused on single SNPs, but SNP-SNP interactions are suggested to reveal crosstalk between SNPs (genes) for increasing power to predict disease risk.

Using the 2,253 AA PCa patients and 2,423 AA controls, SNP main effects and SNP-SNP interactions were evaluated among 205 SNPs, passed quality control in chromosomal region 8q24. Region 8q24 has been shown to be an area of great interest due to numerous variants found to be more common in AA men in this region. We randomly selected half of the subjects in the discovery set and other half in the validation set. The promising results identified in the discovery set were evaluated in the validation and combined set.

The SNP-SNP interaction analyses were evaluated using SNP interaction pattern identifier (SIPI), which assesses 45 interaction models, by taking non-hierarchical models, inheritance modes, and mode coding direction into consideration. The best model for each SNP pair is chosen based upon Bayesian information criterion (BIC). There were 79 SNP-SNP pairs identified by SIPI associated with PCa (p<0.001 in the combined set).
Among top pairs, there were two super SNPs (rs16902359 and rs9642880) in CASC11, which were involved in 56 and 9 pairs, and 59 pairs involved interactions between CASC11 and PVT1. Both genes have been shown to be associated with PCa risk, but interactions between these two genes have not been reported.

Our study has demonstrated that SIPI is a powerful and thorough tool that can be used to detect SNP-SNP interactions because SIPI considers non-hierarchical models, inheritance mode, and 45 different biologically meaningful patterns. Using SIPI, we have identified 79 SNP-SNP pairs of interest in relation to PCa risk of AA men. The interaction of PVT1 and CASC11 provides a great start to future studies in genetic associations where the goal is to build prediction models for clinical use.