GENETICS

Novel prostate cancer susceptibility loci

Prostate cancer shows significant familial association, but known loci have small effects on disease susceptibility, and currently explain very little of the heritable risk. Four papers published in the October 2009 issue of *Nature Genetics* report a number of novel prostate cancer susceptibility loci.

In the first report, Eeles and colleagues build on the findings of a previous genome-wide association study (GWAS), which identified seven loci that were significantly associated with prostate cancer. The researchers investigated 43,671 single nucleotide polymorphisms (SNPs) that had shown evidence of an association with prostate cancer in their original study, using a cohort of 3,650 cases and 3,940 controls from the UK and Australia. They identified 12 novel independent SNPs, which were tested among a further 16,229 cases and 14,821 controls; of these, 9 SNPs in 7 regions showed clear evidence of association with disease, albeit with modest per-allele odds ratios. The identified chromosomal regions were 2p21, 2q31, 4q22, 4q24, 8p21, 11p15 and 22q13.

Gudmundsson and co-workers also followed up the results of a previous GWAS, identifying 4 new variants associated with increased susceptibility to prostate cancer on chromosomes 3q21.2, 8q24.21

(2 variants), and 19q13.2. The researchers also refined a previously reported association on chromosome 11q13, identifying a new SNP that improved the association with prostate cancer.

Finally, two short papers have reported the identification of additional prostate cancer susceptibility loci on chromosome 8q24, the region that has shown the strongest association with disease to date. Yeager and colleagues conducted a GWAS among 10,286 cases and 9,135 controls, and identified an association between the SNP rs620861 and prostate cancer. Al Olama *et al.* investigated SNPs across 8q24 among 5,504 cases and 5,834 controls. They identified 8 SNPs across 5 linkage disequilibrium blocks that were independently associated with disease, including 2 novel loci (rs1006908 and rs620861).

Together, these results add to the growing body of data on genetic susceptibility loci in prostate cancer. However, much work remains to be done in elucidating the genetic basis of the hereditary form of the disease. In fact, Eeles and colleagues note that the susceptibility loci reported to date explain approximately 21.5% of familial risk in prostate cancer, indicating the scale of the challenge ahead.

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Original articles Eeles, R. A. *et al.* Identification of seven new prostate cancer susceptibility loci through a genome-wide association study. *Nat. Genet.* **41**, 1116–1121 (2009) | Gudmundsson, J. *et al.* Genome-wide association and replication studies identify four variants associated with prostate cancer susceptibility. *Nat. Genet.* **41**, 1122–1126 (2009) | Yeager, M. *et al.* Identification of a new prostate cancer susceptibility locus on chromosome 8q24. *Nat. Genet.* **41**, 1055–1057 (2009) | Al Olama, A. A. *et al.* Multiple loci on 8q24 associated with prostate cancer susceptibility. *Nat. Genet.* **41**, 1058–1060 (2009)