

CRT Licensing Opportunity



Prostate Cancer Susceptibility Loci and SNPs

- 7 novel prostate cancer susceptibility loci identified
- These SNPs are independently significant markers of prostate cancer risk
- Opportunity to develop SNP panels to assess prostate cancer risk
- Available for non-exclusive licensing

DIAGNOSTICS | Discovery

October 2009

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Introduction

Prostate cancer is the most commonly diagnosed male cancer and a multitude of studies have reported evidence of familial aggregation. Individuals who have a relative with prostate cancer have a 2 to 3 fold increased risk of developing prostate cancer compared to the population at large. The risk is even higher for those individuals with multiple cases of prostate cancer within their families. Such data suggests that there are genetic factors contributing to prostate cancer susceptibility and development and this is supported by studies with twins (1). The identification of genetic risk factors may allow more widespread screening to identify those individuals at high risk of prostate cancer who should be more closely monitored for the development of clinical disease.

Background

Although there is a clear familial risk associated with prostate cancer only a few susceptibility genes have been identified so far. Together these genes have been predicted to account for only around 10% of the familial risk. Such genes include RNASEL and MSR1 as well as loci such as 8q24 and 17q. The lack of more striking susceptibility genes has been postulated to indicate that the majority of the genetic risk of prostate cancer arises from multiple low penetrance genes/polymorphisms. Genome Wide Association Studies (GWAS)

have now been used in many diseases to identify disease related loci and when sufficiently powered such studies can also identify low penetrance disease associated genes and single nucleotide polymorphisms (SNPs). Diagnostics based on panels of such genes/polymorphisms may be able to identify high risk individuals for whom increased clinical monitoring may be justified.

The Technology

Dr Eeles and colleagues recently published an exciting study identifying seven new loci and polymorphisms linked to prostate cancer susceptibility (2).

The study involved two phases, the first of which contained 1854 clinically diagnosed prostate cancer cases and 1894 normal controls. Analysis of over 500,000 SNPs led to the identification of prostate cancer susceptibility polymorphisms and these candidates were then tested against a pool of 3268 cases and 3366 controls to confirm the associations. Of the SNPs identified 7 were independently significant in terms of their association with prostate cancer susceptibility (see table).

SNP	Heterozygote Odds Ratio	Homozygote Odds Ratio	Significance (P value)
rs10993994	1.15	1.61	8.7×10^{-29}
rs2660753	1.10	2.09	2.7×10^{-8}
rs7920517	1.15	1.49	5.4×10^{-19}
rs2735839	0.80	0.85	1.5×10^{-18}
rs6465657	1.03	1.27	1.1×10^{-9}
rs9364554	1.26	1.24	5.5×10^{-10}
rs7931342	0.84	0.71	1.7×10^{-12}

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A number of these SNPs are linked to sites/genes that may play functional/causative roles in prostate cancer. The most highly associated SNP (rs10993994) is 2bp upstream of the transcriptional start site of the MSMB gene. The MSMB gene encodes PSP94 which is an immunoglobulin binding factor that is produced by prostate epithelial cells and secreted into the seminal fluid. It has been reported that loss of PSP94 is associated with tumour recurrence in patients following prostatectomy (3). The second most significant association is for the SNP rs2735839 which is located between the kallikrein 2 and 3 genes. These genes have also been linked to prostate cancer and proposed as possible screening markers.

Commercial Opportunity

The creation of a panel of prostate cancer susceptibility markers may allow screening to identify individuals at high risk of developing prostate cancer. Such individuals may benefit from closer clinical follow up and management to ensure timely diagnosis and intervention. These SNPs are ideal candidates for inclusion in such a panel and are available for non-exclusive licensing.

Intellectual Property

CRT has a patent application covering 11 SNPs as markers of prostate cancer susceptibility (WO 2009/056862).

References

- 1) Watkins-Bruner *et al.* Relative risk of prostate cancer for men with affected relatives: systematic review and meta-analysis. *Int. J. Cancer* 2003. **107**: 797-803.
- 2) Eeles *et al.* Multiple newly identified loci associated with prostate cancer susceptibility. *Nature Genetics* 2008. **40**(3): 316-321.
- 3) Reeves *et al.* Prognostic value of prostate secretory protein of 94 amino acids and its binding protein after radical prostatectomy. *Clin. Cancer Res.* 2006. **12**:6018-6022.

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