Null Results in Brief

Association between Genetic Polymorphisms of Macrophage Scavenger Receptor 1 Gene and Risk of Prostate Cancer in the Health Professionals Follow-up Study

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Abstract

Background: Macrophage scavenger receptor 1 (MSR1) is involved in chronic inflammation, which is a risk factor for prostate cancer. Association studies assessing the relationship between sequence variants of MSR1 and prostate cancer are inconsistent. We hypothesized that sequence variants of MSR1 were associated with prostate cancer risk.

Methods: In a nested case-control design within the Health Professionals Follow-up Study, we identified 700 participants with prostate cancer diagnosed after they had provided a blood specimen in 1993 and before January 2000. Controls were 700 age-matched men without prostate cancer who had had a prostate-specific antigen test after providing a blood specimen. We genotyped three common (>5%) single nucleotide polymorphisms (SNP) that have been reported previously to be associated with risk of prostate cancer.

Results: None of these MSR1 SNPs nor estimated haplotypes were associated with prostate cancer risk (P for the global test for haplotypes = 0.89). These MSR1 SNPs also did not appear to be associated with higher-grade or advanced-stage prostate cancer.

Conclusion: The association between these sequence variants of MSR1 and the risk of prostate cancer was null. Further study of aggressive prostate cancer may be warranted, as we had limited power to assess these. (Cancer Epidemiol Biomarkers Prev 2008;17(4):1001–3)

Macrophage scavenger receptor 1 (MSR1) is located on chromosome 8p22 (1, 2) and was highly expressed in the kidney, colon, prostate, breast, and heart.3 Its isoforms are involved in host defense (inflammation, innate and adaptive immunity; ref. 3). A recent meta-analysis (4) reported five common sequence variants (PRO3, INDEL1, IVS5-59, P275A, and INDEL7) moderately associated with prostate cancer risk. Studies reported after the previous meta-analysis showed inconsistent findings for P275A (5, 6). Abundant evidence supports a possible link between chronic intraprostatic inflammation and risk of prostate cancer (7). MSR1 plays a role in the innate immune response to pathogen infection and therefore may relate to prostate cancer risk.

The characteristics of the study population are available elsewhere (8). The three single nucleotide polymorphisms (SNP) in MSR1 associated previously with risk of prostate cancer were genotyped (Table 1). SNP IVS5-59 was out of Hardy-Weinberg equilibrium among controls (P = 0.01). The internal blinded quality-control specimens showed no evidence of genotyping error. Therefore, we retained IVS5-59 in the statistical analyses.

The three single nucleotide polymorphisms (SNP) in MSR1 associated previously with risk of prostate cancer were genotyped (Table 1). SNP IVS5-59 was out of Hardy-Weinberg equilibrium among controls (P < 0.01) but not among cases (P = 0.11). The internal blinded quality-control specimens showed no evidence of genotyping error. Therefore, we retained IVS5-59 in the statistical analyses.

The three common haplotypes were associated with prostate cancer risk (Table 2). The P value for the global test comparing the case and control distribution of the three common haplotypes was 0.89. Statistical analyses showed that none of the three common SNPs or their haplotypes was associated with prostate cancer risk (Table 2). Prostate cancer family history, body mass

Received 8/12/07; revised 10/26/07; accepted 2/8/08.

Grant support: NIH grants U01 CA98233 and CA55075.

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doi:10.1158/1055-9965.EPI-07-0744

Cancer Epidemiol Biomarkers Prev 2008;17(4). April 2008

http://genome.ucsc.edu/cgi-bin/hgGene?hgsid=66892801&db=hg16&hgg_gene=D90187&hgg_chrom=chr8&hgg_start=15977333&hgg_end=16060514

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Table 1. Characteristics of MSR1 SNPs

<table>
<thead>
<tr>
<th>SNP</th>
<th>Nucleotide change</th>
<th>Location</th>
<th>rs #</th>
<th>Controls Minor allele frequency (%)</th>
<th>Hardy-Weinberg equilibrium P</th>
<th>Cases Minor allele frequency (%)</th>
<th>Hardy-Weinberg equilibrium P</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRO3</td>
<td>A→G</td>
<td>Promoter</td>
<td>rs433235</td>
<td>8.8</td>
<td>0.08</td>
<td>8.4</td>
<td>0.25</td>
</tr>
<tr>
<td>IVS5-59</td>
<td>C→A</td>
<td>Intron 5</td>
<td>N/A</td>
<td>4.9</td>
<td>&lt;0.01</td>
<td>5.1</td>
<td>0.11</td>
</tr>
<tr>
<td>P275A</td>
<td>C→G</td>
<td>Exon 6</td>
<td>rs3747531</td>
<td>5.1</td>
<td>0.95</td>
<td>6.2</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Table 2. OR between MSR1 SNPs and haplotypes and the risk of prostate cancer

<table>
<thead>
<tr>
<th>SNP</th>
<th>Prevalence among controls, % (95% CI)</th>
<th>Global test P = 0.89</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 copies</td>
<td>1 copy</td>
</tr>
<tr>
<td>PRO3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IVS5-59</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P275A</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NOTE: From left to right, the haplotypes above were composed of PRO3, IVS5-59, and P275A.

*P tested the null hypothesis: OR1 copy = OR2 copies = 1.
rise to the cases and were composed of 94% Caucasians. Results were similar after the exclusion of non-Caucasians.

Chronic intraprostatic inflammation has been reported to increase the risk of prostate cancer (7). Our previous study (8) showed that variants in the innate immune gene TLR4 played a role in prostate cancer susceptibility. However, in our study and most previous studies, no association between sequence variants of MSR1 and prostate cancer risk has been observed.

Acknowledgments
We thank Monica Coleman for assistance, Pati Soule and Ana-Tereza Andrade for DNA sample extraction, and the Partners High-Throughput Genotyping Center (Dr. David Kwiatkowski, Alison Brown, and Maura Regan) for genotyping.

References
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