BRIEF COMMUNICATION

p53 and Genetic Susceptibility to Cervical Cancer

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In a recent report, Storey et al. (1) provide compelling experimental evidence that two common polymorphic variants of the p53 tumor suppressor protein differ in their susceptibility to degradation mediated by the E6 oncoprotein of human papillomavirus (HPV). Specifically, the p53 protein with arginine at codon 72 was shown to be more susceptible to E6-induced degradation in vivo than p53 with proline at codon 72. Remarkably, homozygosity for the allele encoding arginine was found at a significantly higher frequency in the germlines of individuals affected by either of two HPV-associated cancers, squamous carcinoma of the cervix or cutaneous carcinomas in renal transplant recipients, than in the germlines of a control population. Storey et al. conclude that individuals homozygous for the arginine-encoding allele of p53 are seven times more susceptible to HPV-associated cervical tumorigenesis than heterozygotes.

Squamous carcinoma of the uterine cervix is the most common gynecologic cancer encountered worldwide (2), and these data provide the first evidence for a possible genetic susceptibility to this malignancy. Furthermore, given that many sexually active females are transiently infected with HPV (3) and that virtually all squamous carcinomas of the cervix are associated with HPV infection (4), the public health implications of these findings are potentially enormous.

As the numbers of cervical cancer case patients (n = 30) and control subjects (n = 41) were rather small and limited the power of the study described above (1), we attempted to confirm these findings in a larger case-control analysis. As shown in Fig. 1, genotypes at p53 codon 72 were determined by direct sequence analysis of DNA from 205 individuals. Case patients consisted of 105 individuals treated at this institution for pathologically confirmed squamous cell carcinoma of the cervix. To control for ethnic, geographic, and socioeconomic factors, the control population consisted of 100 gynecology patients also treated at this institution over the same time period, none of whom had any history of squamous cancers of the reproductive tract or genitalia.

As shown in Table 1, the genotype frequencies at p53 codon 72 did not differ substantially between the two groups of patients studied (two-sided P = .6, chi-square). Logistic regression analysis indicated that the relative risk of cervical cancer associated with homozygosity for arginine at p53 codon 72, estimated as an odds ratio, was 0.7 (95% confidence interval = 0.4–1.3, two-sided P = .3). Statistical analyses were performed using the StatView software package (SAS Institute, Inc., Cary, NC). Notably, the frequency of individuals homozygous for arginine was lower in our cervical cancer population than in that reported by Storey et al. (1), while the frequency in our control group was higher, suggesting that those data previously reported may have represented an artifact of small sample size. In conclusion, our data do not support the hypothesis that the p53 codon 72 polymorphism represents a genetic susceptibility factor for squamous carcinoma of the cervix.

REFERENCES


Table 1. Genotype frequencies for p53 codon 72 in cervical cancer patients and control subjects

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Cancers, n=105</th>
<th>Controls, n=100</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arginine</td>
<td>50 (0.48)</td>
<td>55 (0.55)</td>
</tr>
<tr>
<td>Arginine/proline</td>
<td>41 (0.39)</td>
<td>35 (0.35)</td>
</tr>
<tr>
<td>Proline</td>
<td>14 (0.13)</td>
<td>10 (0.10)</td>
</tr>
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</table>

*Values = numbers of individuals corresponding to each of three possible genotypes for the codon 72 polymorphism of p53. Numbers in parentheses = relative frequencies of each genotype.

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