Letters to the Editor

Contrasting Frequencies of CCR5Δ32 and CCR2-64I Alleles in the Tunisian Population

To the Editor: The human CC-chemokine receptor 5 (CCR5) is the major coreceptor on CD4+ cells for most of the transmitting strains of HIV-1 (1,2). The complete absence of the CCR5 protein expression on the surface of CD4+ T cells in approximately 2% of the white population, due to homozygosity for a 32-nucleotide long deletion in the CCR5 coding region (CCR5Δ32 allele), has been shown to be a protective mechanism against HIV-1 transmission in a number of HIV-1–exposed but uninfected individuals (3-6). Furthermore, CCR5Δ32 heterozygotes were shown to progress more slowly in several AIDS study cohorts (5,6). Furthermore, a conservative substitution of a valine for an isoleucine at position 64 in the coding region of the CCR2 (CCR264I), was also shown to be protective against disease progression (7). Interestingly, CCR264I was found to be in strong linkage disequilibrium with CCR5-59653T, a mutation in the CCR5 regulatory region (8). More recently, it has been reported that infected individuals homozygous for a multisite haplotype of the CCR5 regulatory region containing the promoter allele CCR5P1 progress to AIDS more rapidly than those with other CCR5 promoter genotypes (9).

We have studied the frequencies of the CCR5Δ32, CCR2-64I, and CCR5-59653T alleles in 145 healthy HIV-1 uninfected Tunisian individuals by the spectral genotyping assay (10). We found that the CCR5Δ32 allele is significantly less frequent (Fisher exact test p value <.0001) compared with previous studies on white populations (8). The genotype distribution is in equilibrium as predicted by the Hardy-Weinberg equation (p = .8998) showing that no strong selection process is currently acting against the population (Table I). In contrast to the CCR5Δ32 allele, the CCR2-64I allele is significantly more frequent in the Tunisian population (Fisher exact test p value = .0108). Furthermore, the CCR-59653T mutant allele is in complete linkage disequilibrium with CCR2-64I as previously reported (8).

TABLE I. Percentages of CCR5 and CCR2 genotypes

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Number</th>
<th>Frequency (%)</th>
<th>HWE*</th>
<th>χ² (p-value)</th>
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<tbody>
<tr>
<td>CCR5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>145</td>
<td>1.03</td>
<td>0.0158</td>
<td>.8998</td>
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<tr>
<td>CCR5+/-</td>
<td>143</td>
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<tr>
<td>CCR5-Δ32</td>
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<td></td>
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<tr>
<td>CCR5-Δ32Δ32</td>
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<tr>
<td>CCR2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>145</td>
<td>19.31</td>
<td>1.9101</td>
<td>.1670</td>
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<tr>
<td>CCR2-+/-</td>
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<tr>
<td>CCR2-664I</td>
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<td>CCR2-64I/64I</td>
<td>8</td>
<td></td>
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</tr>
</tbody>
</table>

*Hardy-Weinberg equilibrium; the value of χ², with the associated p value for significant departures.

Our results of the CCR5Δ32 and CCR264I/CCR5-59653T allele frequency obtained in the Tunisian population are consistent with results from previously published studies indicating that CCR5Δ32 allele frequencies decrease in their frequency from Northern European to sub-Saharan populations (3-6,11) with intermediate values found in Mediterranean populations (12-14). In contrast, the CCR264I mutation, which is in complete linkage disequilibrium with the CCR5-59653T, shows an inverse gradient, with higher values in the south and lower values in the north (15). The reason for the differences in CCR5Δ32 and CCR264I alleles frequencies observed in the Tunisian population compared with other white populations from Central or Northern Europe is unknown (15). One possible explanation, however, is that the modern Tunisian population is a mosaic resulting from the melding, through 3,000 years of history, of several populations such as Berber, Phoenician, Roman, Vandalian, Arabian, Black African, Spanish, Turkish, French, and other populations.

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