References


The frequency of allele \(a^{LELY}\), a low expression allele of the gene encoding erythroid spectrin \(\alpha\)-chain, in the Greek population

Sir, \(a^{LELY}\), a low expression allele of the SPTA1 gene, encodes the \(\alpha\)-chain of erythroid spectrin.\(^1\) It is characterized by a \(C\rightarrowG\) mutation at position \(\alpha1857\) in exon 40;\(^2\) it is functionally neutral, but yields major peptide map abnormalities,\(^3\) and a \(C\rightarrowT\) (nt12) mutation in intron 45. This second mutation is responsible for the partial skipping of exon 46,\(^4\) which is essential for the nucleation of spectrin \(\alpha/\beta\)-chain dimerization. Although \(a^{LELY}\) does not cause symptoms in either heterozygotes or homozygotes, it enhances the expression of deleterious \(a\)-alleles and, thus, has clinical importance.

Allele \(a^{LELY}\) is encountered in distinct ethnic groups, Caucasians, African Blacks, Japanese, Chinese, Brazilians, and Parakana Indians, with a rather uniform frequency.\(^5\) Among French Caucasians its frequency was estimated to be 0.59. We investigated 175 individuals randomly selected from all parts of Greece. Exon 40 and intron 45 mutations were screened using a polymerase chain reaction.\(^6\) Chi-square test was used to determine whether frequencies in certain groups were significantly different.\(^7,8\) The frequency of allele \(a^{LELY}\) between distinct ethnic groups considered by pairs (Caucasians [Greek + French]) vs. non-Caucasians.\(^6,7\)

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>(u)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caucasians</td>
<td>454</td>
<td>0.289</td>
</tr>
<tr>
<td>Africans</td>
<td>86</td>
<td>0.209</td>
</tr>
<tr>
<td>Japanese</td>
<td>100</td>
<td>0.20</td>
</tr>
<tr>
<td>Chinese</td>
<td>36</td>
<td>0.222</td>
</tr>
<tr>
<td>Brazilians</td>
<td>108</td>
<td>0.241</td>
</tr>
<tr>
<td>Parakana Indians</td>
<td>82</td>
<td>0.159</td>
</tr>
</tbody>
</table>

Abbreviations: \(n\): numbers of SPTA1 alleles investigated; \(u\): frequencies of allele \(a^{LELY}\) in individual populations. The frequencies of allele \(a^{LELY}\) were significantly different \(\pm 0.05\) between any particular pair of groups.

![Figure 1. The allelic distribution of \(a\)/\(\alpha\) (1), \(a\)/\(a^{LELY}\) (2) and \(a^{LELY}\)/\(a^{LELY}\) (3) in the Greek population (A: values as percentages) and of the \(a\) (1) and \(a^{LELY}\) alleles (2) (B: values as frequencies).](image-url)
different (p<0.05) from the overall mean frequency of allele α-LELY, and whether frequencies were significantly different (p<0.05) within any particular pair of groups, the m±2s interval being used in all cases. We found that the distribution of α-α, α/α and α/αLELY and α/αLELY/αLELY individuals was: 91(52%), 71(41%) and 13(7%), respectively (Figure 1a). Out of 350 SPAT1 genes (Figure 1b), we found 97αLELY alleles, which corresponds to a frequency of 0.28. Exon 40 and exon 45 mutations were always found to be linked. The frequency of allele αLELY in Greek Caucasians was thus almost identical to that recorded among French Caucasians. The overall mean of all available frequencies,3,6 including this work, (n=866 Caucasians) is α-α=0.22±0.087. The only statistically significant difference (0.01<p<0.05) was that for the pair of Caucasians and Parakana Indian groups (Table 1).

The Greek and French populations are both of Caucasian origin1 and thus could be expected to have similar frequencies of the α-LELY and this expectation is supported by all experimental evidence (ref. #5 and present study). Allele αLELY also appears with similar frequencies in remote ethnic groups3,6 yet not as uniform as within Caucasians. The significant difference between the Caucasian population and Parakana Indians (0.01<p<0.05), noted here, shows that the α-LELY polymorphism, although relatively constant throughout the world, is less so in very isolated populations. Parakana Indians form a very ancient population and have a very restricted range of polymorphisms for several genetic markers.6,8 αLELY is deleterious only in trans of SPAT1 alleles that cause HE and may reach a non-negligible proportion of the population.9 This issue has not yet been evaluated in Greek populations.

The presumably universal character of αLELY is consistent with a very ancient origin. The present study underscores the high stability of allele αLELY among Caucasians and even non-Caucasians with exception of the Parakana Indians.

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SPAT1 gene, low expression allele αLELY, Greek population

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Acute myeloid leukemia occurring in a patient with polycythemia vera in treatment with hydroxyurea

Sir,

Hydroxyurea is a non-alkylating chemotherapeutic agent used in the treatment of patients with polycythemia vera (PV). The leukaemogenic risk associated with treatment with hydroxyurea alone is considered to be relatively low but the probability of development of acute leukaemia has been recognized as a long-term side-effect.1 We report the case of a patient with PV who developed acute myeloblastic leukemia (AML) after three years of treatment with hydroxyurea.

A 62-year-old man was admitted because of leukocytosis and thrombocytosis in February 1995. Clinical examination revealed only splenomegaly of 3 cm. Full blood count was erythrocytes 5.630×10^12/L; hemo-

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References