β thalassaemia mutations in the Turkish population

Only sparse information is available at present on the molecular pathology of the β thalassaemias in the Turkish population. In this study, we have carried out haplotype analysis on the β globin gene cluster and characterised the β thalassaemia mutations by oligonucleotide hybridisation in 10 Turkish patients with thalassaemia major, who have been followed at the Department of Pediatrics at Ankara University. Haplotype analysis and oligonucleotide hybridisation were carried out as previously described.1 2 We used three oligoprobes complementary to the most frequent β thalassaemia mutations in Mediterraneans, namely the G-A substitution at position 110 of the first intervening sequence of the β globin gene (β+ IVS-1, nt 110), the C-T substitution at codon 39 (β39), and the T-C substitution at position 6 of IVS-1 (β+ IVS-1, nt 6). Oligonucleotide analysis showed the β+ IVS-1, nt 110 mutation in 13 out of 20 (65%) β thalassaemia chromosomes investigated. In the remaining chromosomes the presence of β39 and the β+ IVS-1, nt 6 mutations was excluded (table). A representative autoradiogram is shown in the figure. Four patients were homozygous for the β+ IVS-1, nt 110 mutation and five were compound heterozygotes for this mutation and a different β thalassaemia mutation, not yet characterised. The β+ IVS-1, nt 110 mutation was contained without exception in haplotype 1 according to the nomenclature of Orkin et al.2 The polymorphic AvaI site in the ψβ globin gene, which has been found to be in strong linkage disequilibrium with the β+ 110 mutation, was absent in all of the β thalassaemia chromosomes containing the β+ IVS-1, nt 110 mutation investigated. Haplotype 1 was also found frequently in normal chromosomes (18 out of 38 investigated), but in these chromosomes the AvaI ψβ polymorphic site was absent in three out of 76 chromosomes analysed.

In conclusion, this study shows that the most frequent β thalassaemia allele in the Turkish population is the β+ IVS-1, nt 110 mutation, which is the most common β thalassaemia mutation in the majority of the high risk regions of the Mediterranean area. The β+ 110 mutation was found without exception in haplotype 1, as has already been observed in several Mediterranean populations, confirming the strong association between haplotypes and β thalassaemia mutations. In this population, oligonucleotide analysis with an oligoprobe complementary to the β+ 110 mutation may allow prenatal diagnosis to be made in approximately 40% of the pregnancies at risk and will exclude thalassaemia major in the large majority of the remaining pregnancies. In the Turkish population, as in Cypriots, the AvaI ψβ polymorphic site is in strong linkage disequilibrium with the β+ 110 mutation. Linkage analysis between this site and β thalassaemia may also be used for prenatal diagnosis in those couples with previous normal or affected children.

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TABLE

Association of specific β thalassaemia mutations and chromosomal haplotypes in the Turkish population.

<table>
<thead>
<tr>
<th>Haplotypes</th>
<th>HincII</th>
<th>HindIII</th>
<th>HincII</th>
<th>AvaII</th>
<th>BamIII</th>
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</table>

*Oligonucleotide analysis excluded the presence of the β39 and the IVS-1, nt 6 mutations.

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References


A new case of (Y;1) balanced reciprocal translocation in an infertile man with Hodgkin’s disease

The proband was a 31 year old man with no children after two years of marriage. His two brothers, uncles, and aunts were fertile. There was no history of infectious disease or trauma. He was 1.73 m tall, weighed 65 kg, and had no dysmorphic features. Physical examination showed slight testicular hypotrophy (12 and 15 ml) and a varicocele.
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