CORRESPONDENCE

THE T → C SUBSTITUTION AT NUCLEOTIDE +1570 OF THE β-GLOBIN GENE IS A POLYMORPHISM

To the Editor:

In the March 15, 1992 issue of *Blood,* we reported on an Irish family in whom five members had β-thalassemia trait phenotype. All five affected individuals were found to have a novel T → C substitution in nucleotide (nt) +1570 relative to the β-globin gene cap site, or 12 bp 5′ upstream of the AATAAA polyadenylation signal in the 3′ noncoding region.[1] We postulated that this substitution may lead to destabilization of the encoded β-globin mRNA.

Recently, Russell and Liebhaber[2] introduced the T → C substitution into a normal β-globin gene. Both the mutated and the normal β-globin genes were cotransfected into murine erythroleukemia cells, and transiently expressed. There was no difference between the mRNA levels of the mutated and the normal β-globin genes.[2] Furthermore, Divoky et al[3] discovered that a black man with hemoglobin S (HbS)-β°-thalassemia and his two relatives with β-thalassemia trait were found to have the same T → C substitution as well as the known IVSII-654 C → T β°-thalassemia mutation. The IVSII-654 mutation is common in the Chinese population.[4]

We have now re-examined the Irish family. We confirmed by polymerase chain reaction and direct nucleotide sequencing that all five family members with β-thalassemia trait phenotype are carriers of both the T → C substitution as well as the IVSII-654 C → T β°-thalassemia mutation, indicating that these two substitutions are linked in this family.

We have also examined nine unrelated Chinese individuals who are carriers of the IVSII-654 mutation. None has the T → C substitution. A similar finding has been observed by Divoky et al.[3] In addition, the T → C substitution has recently been reported to be present in some Czechoslovakian families.[5] In one adult with β-thalassemia trait phenotype, the T → C substitution occurs in trans to the common IVSI-110 G → A β^+-thalassemia mutation.[5]

In conclusion, the T → C substitution at nt +1570 of the β-globin gene represents a polymorphism. The β-thalassemia trait phenotype in the reported Irish family is caused by the IVSII-654 C → T β°-thalassemia mutation.

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