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. We postulated that this substitution may lead to destabilization of the encoded β-globin mRNA. Recently, Russell and Liebhaber 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. Furthermore, Divoky et al discovered that a black man with hemoglobin S (HbS)-βthalassemia 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 Po-thalassemia mutation. The IVSII-654 mutation is common in the Chinese population.

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. In addition, the T → C substitution has recently been reported to be present in some Czechoslovakian families. 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.

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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REFERENCES

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