A NEW CODON 71 (+T) MUTANT RESULTING IN β° THALASSEMIA

To the Editor:

Over 50 different mutations have been described causing β thalassemia, and each ethnic group carries its own common set of mutants. Molecular characterization showed that even the same mutant arose as independent events in different parts of the world. In a previous study of 93 unrelated β thalassemia genes in South China, we found that four mutations accounted for 87% of the cases. Of the 10 undefined β thalassemia mutations, all but one had since been identified using polymerase chain reaction (PCR) amplification of genomic DNA followed by oligonucleotide hybridization or direct sequencing. These included the following known mutants: 3 codon 41/42 (-TCTT), 1 IVS-2 nt 654 (C→T), 1 codon 17 (A→T), 1 codon 71/72 (+A), and 2 recently described frameshift mutations at codon 14/15 (+G). We now report another new mutant that lies in codon 71 of the β gene.

Direct sequencing of PCR-amplified genomic DNA was made as previously described and the sequence showed an insertion of T in codon 71 (Fig 1). This mutation was confirmed by allele-specific oligonucleotide hybridization using 5'-end labeled probes. S'-TCG GTG CCT TTT AGT GAT G-3' and 5'-CAT CAC TAA AGG CAC CGA G-3', being β and β° probes, respectively.

The patient, aged nine years, was transfusion-dependent since the age of 7 months. She is compound heterozygous for codon 71 and IVS-2 nt 654 with haplotypes 2 and 1 (Chinese), respectively. The β thalassemia gene was inherited from her father who originated from Po On County in the Guangdong Province of South China.

This new codon 71 mutant occurred in a chromosomal background similar to the codon 71/72 mutation described by Cheng et al. These two variants with insertions of T or A at or post codon 71 (TTT) are the only T/A insertion so far reported in the β globin gene. They create termination codons, TAG and TGA, respectively, immediately downstream, thereby giving rise to β° thalassemia.

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REFERENCES

A new codon 71 (+T) mutant resulting in beta zero thalassemia [letter]

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