Hinf I polymorphism 3' to the human β -globin gene detected by the polymerase chain reaction (PCR)

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SOURCE: 741 bp PCR amplification product of human β -globin gene 3'-flanking sequences. 5' oligomer (KZ53): TGGATTCTGCCTAAATAAAA (poly(A)-addition signal underlined); 3' oligomer (SP11): GGGCCTATGATAGGGTAAT (see Figure).

POLYMORPHISM: Nucleotide sequence analysis of a cloned β -globin gene previously revealed an A to T transversion which destroys a Hinf I site located approximately 340 bp 3' of the poly(A) addition site¹. Hinf I digestion of PCR-amplified DNA generates fragments of: 128 + 213 bp if site is present (+), 341 bp if absent (-); 244 + 154 bp constant fragments.

FREQUENCY: 75 chromosomes from unrelated Black, Caucasian and Oriental individuals with β^A , β^S , and β -thalassemia alleles: f(+)=0.67 and f(-)=0.33. The Hinf I polymorphism is in linkage disequilibrium with a BamHI polymorphism.² On all chromosomes analyzed (13 unrelated individuals and 9 nuclear families), both sites were either present or absent. The Hinf I site is thus a marker for framework 2 β -globin genes².

MENDELIAN INHERITANCE: Confirmed in 9 nuclear families (Figure).

OTHER COMMENTS: Unlike the Bam HI polymorphism which is located 3' within an L1 repetitive element, the Hinf I polymorphism can be utilized for prenatal diagnosis of hemoglobinopathies by PCR amplification and haplotype analysis with the Hind III- $G\gamma$, Hind III- $A\gamma$, Rsa I-5' β , and Ava II- β sites within the β -globin gene cluster, eliminating the added time and exposure to radioactivity needed for Southern blot hybridization.

REFERENCES: 1) Semenza, G.L. *et al.* (1984) Cell 39:123-128; 2) Orkin, S.H. and Kazazian, H.H., Jr. (1984) Ann. Rev. Genet. 18:131-171.

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Figure. Left, map with oligonucleotide primer sites (vertical lines) and Hinf I sites (arrows). Right, gel with Hinf I digests of PCR products from DNA of (M) +/- mother; (P) +/- father; (F) +/- fetus; and (S) PhiX174-HaeIII size markers.