Two BglII RFLPs of the human α -globin gene cluster in the American sickle cell population

S.H.Embury*, T.Blachman, G.L.Kropp, J.K.Suzuki and M.Boyle

Division of Hematology, The Medical Services, San Francisco General Hospital and University of California and Northern California Comprehensive Sickle Cell Center, Building 100, Room 263, SFGH, San Francisco, CA 94110, USA

SOURCE/DESCRIPTION: Human α -globin cDNA cloned into plasmid pMB9 (JW101) was used as a hybridization probe for assessing the α -globin genotypes of 2271 Americans with sickle cell anemia.

POLYMORPHISM: The normal duplicated human α -globin genes, $\alpha 2$ and $\alpha 1$, reside on separate Bgl II fragments, each of which is cleaved by Hin dIII (1), as shown below. Both α loci reside on a single 14 kb Bam HI fragment. We performed single Bgl II and Bam HI digests to detect α -globin gene deletions in 2271 subjects enrolled in the National Cooperative Study of Sickle Cell Disease (NCSSCD).

In addition to gene deletions and duplications, the two Bgl II RFLP shown in the figure were found. One, resulting in greater density of the 7.0 kb Bgl II fragment compared to the 12.5 kb fragment, was seen in 29 subjects. An additional 5.0 kb fragment found on double digestion with Bgl II + Hin dIII demonstrated a polymorphic Bgl II site in the $\alpha 2$ -specific Bgl II fragment (2). A second RFLP, yielding a 5.0 kb fragment in addition to the normal Bgl II fragments, was found in 10 subjects. On double Bgl II + Hin dIII digestion an additional 3.0 kb fragment seen showed that this RFLP was due to a polymorphic Bgl II site in the $\alpha 1$ -specific Bgl II fragment. Both RFLP were in DNA having the normal 14 kb Bam HI fragment; 2 of 29 $\alpha 2$ -RFLP were *in trans* to a single α locus.

FREQUENCY: The $\alpha 2$ -RFLP gene frequency of 0.0064 may have been underestimated due to failure to detect differences in band intensities in single Bgl II digests. The $\alpha 1$ -RFLP gene frequency was 0.0022.

NOT POLYMORPHIC FOR: Bam HI.

CHROMOSOMAL LOCATION: The human α -globin genes reside on the short arm of chromosome 16 (3).

MENDELIAN INHERITANCE: The $\alpha 2$ -specific RFLP occurs in linkage disequilibrium (2), and the mother of one subject with the $\alpha 1$ -specific RFLP had this RFLP, suggesting their Mendelian inheritance.

PROBE AVAILABILITY: Contact Stephen Embury.

COMMENTS: These RFLP may be useful for α -globin gene haplotyping.

REFERENCES: 1. Embury, S.H. *et al.* J Clin Invest (1980) 66: 1319-1325. 2. Wainscoat, J.S. *et al.* Am J Hum Genet (1983) 35: 1086-1089. 3. Breuning, M. H. *et al.* Hum Genet (1987) 76: 287-289.

ACKNOWLEDGEMENTS: We acknowledge the support of the (NCSSCD) and the N.I.H. (HL 20985), B. Forget for JW 101, and M. Steinberg for the DNA from the mother of a subject with the $\alpha 1$ -RFLP.

*To whom correspondence should be addressed