To the Editor:

Diamond-Blackfan anemia (DBA) is a congenital hypoplastic anemia characterized by decreased erythroid progenitors in the marrow. Human DBA in some ways resembles the anemia of Sl and W mutant mice, which respectively result from defects of the genes encoding mast/stem cell growth factor (Mgf) and its tyrosine kinase receptor (Kit). However, we previously noted that humans with pathologic mutations of the KIT gene do not exhibit anemia. Furthermore, Southern blot hybridization analyses of 22 patients with DBA failed to identify alterations of the MGF and KIT genes, and nucleotide sequence analysis of MGF and KIT cDNAs from two of these patients likewise showed no abnormalities.

We have screened an additional eight patients with DBA for single-base substitutions in the KIT and MGF genes, and also found no abnormalities. Six of these cases were sporadic, one was apparently autosomal dominant, and one was apparently autosomal recessive. Four of these patients are among those previously studied by Southern blot hybridization (DB, CB, BS, and NM in ref 3). The 21 exons (and surrounding noncoding sequences) of the KIT gene and the 9 exons of the MGF gene were amplified from genomic DNA of each patient by the PCR and analyzed by simultaneous heteroduplex/single-strand conformation polymorphism (SSCP) analysis. Three patients had aberrant patterns, all in the KIT gene. However, DNA sequence analyses showed that all three resulted from silent DNA polymorphisms: C versus T at base 56 of IVS1, codon Leu862CTG→CTC, and codon Ile935ATT→ATA.

A total of 10 patients has now been screened for pathologic single-base substitutions of the KIT and MGF genes without detecting any abnormalities. Of these 10 cases, seven were sporadic, two appeared autosomal dominant, and one appeared autosomal recessive. These negative data strongly suggest that the various forms of human DBA do not result from abnormalities of either the KIT or MGF genes, but instead result from defects of genes that have yet to be identified.

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REFERENCES
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Lack of mutations of the MGF and KIT genes in Diamond-Blackfan anemia [letter]

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