CONCISE REPORT

Detection of Hemophilia A Carriers Using Intragenic Factor VIII:C DNA Polymorphisms


A DNA polymorphism for an XbaI site in intron 22 of the human factor VIII:C gene extends the utility of DNA methods for carrier detection in families segregating for hemophilia A. While the DNA polymorphism detected by a BglI site in intron 18 of the factor VIII:C gene was informative for 41% of females studied, the BglI/intron 25 polymorphism provided no additional information because of apparent linkage disequilibrium. In contrast, the XbaI intron 22 polymorphism was useful in 53% of women who were informative (homozygous) for either the BglI or BgII polymorphisms. Using the BglI/intron 18 and XbaI/intron 22 intragenic polymorphisms, we could provide highly accurate information for 68% of women we studied who were at risk for carriership. The carrier status of the remaining 32% could be determined utilizing the closely linked TaqI/St14 DNA polymorphism.

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RESULTS AND DISCUSSION

Frequency of informative RFLPs. A woman was considered to be informative if she was heterozygous for an RFLP and the linkage phase of the DNA polymorphism and the normal or abnormal factor VIII:C allele could be established. The extragenic TaqI/St14 RFLP, which is closely linked, was informative in 103/106 (97%) of women studied.

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