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MspI polymorphism in the 3′ flanking region of the human factor VIII gene

Hagop Youssoufian, Deborah G.Phillips, Haig H.Kazazian, Jr and Stylianos E.Antonarakis

Genetics Unit, Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, MD 21205, USA

SOURCE AND DESCRIPTION OF CLONE: p625.3, a 5.4 kb EcoRI fragment from the 3′ flanking region of the human factor VIII (FVIII) gene that was derived from a genomic library[1] and subcloned into pUC13.

POLYMORPHISM: Msp I identifies two alleles with DNA fragments at 7.5 kb (-) or at 4.3 kb and 3.2 kb (+). Also seen is a constant fragment at 3.0 kb.

FREQUENCY: Unrelated individuals studied: 22 females, 23 males (67 X-chromosomes)

7.5 kb allele	68%
4.3 kb and 3.2 kb allele	32%

NOT POLYMORPHIC FOR: TaqI

CHROMOSOME LOCALIZATION: The FVIII gene is localized to Xq28

FVIII GENE LOCALIZATION: The variant MspI site is mapped in the 3′ flanking region of exon 26 about 72 kb 3′ to a BclI polymorphic site[1], 54 kb 3′ to an XbaI polymorphic site[2], and 9 kb 3′ to a BglI polymorphic site[3].

PROBE AVAILABILITY: Dr. R.M. Lawn, Genentech, Inc.

OTHER COMMENTS: The MspI polymorphism is in linkage disequilibrium with all previously described polymorphic sites in the FVIII gene. There was complete concordance between the MspI and BclI polymorphisms among 44 chromosomes examined (28 were + +, 16 were - -). Since the MspI polymorphism is easier to detect than the BclI polymorphism, it is useful in carrier detection and prenatal diagnosis.

REFERENCES: 1) Gitschier, J. et al (1984) Nature 312: 326-330; 2) Wion, K.L. et al (1986) Nucl. Acids Res. 14: 4535-4542; 3) Antonarakis, S.E. et al (1985) New Eng. J. Med. 313: 842-848.

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