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# Probing the human genome with minisatellite-like sequences from the human coagulation factor VII gene

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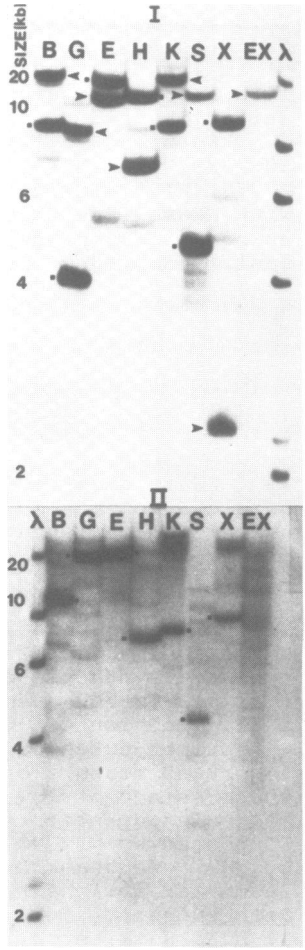
The human factor VII gene contains five minisatellite-like elements (MLEs), one in the untranslated portion of the eighth exon and four in introns (1). Two of the MLEs, one in exon 8 and one in intron B, consist of tandem repeats related to similar consensus sequences [ATGCACACACACAGG] and [(T/A)CACCTCACACTCACAGG] respectively. The monomer elements of the exon 8 MLE are loosely related to its consensus, while those of the intron B MLE are more faithful duplications of its core sequence.

We isolated two restriction fragments, each ~1kb in length, one containing the intron B MLE and one containing the exon 8 MLE. The fragments were labeled with P32 by nick translation and used to probe total human genomic DNA digested with BamHI (B), BglII(G), EcoRI (E), HindIII (H), KpnI (K), SstI (S), XbaI (X) or EcoRI+XbaI (EX). The electrophoretically separated restriction fragments were transfered to nitrocellulose filters and then hybridized to the MLE probes at 42C in 40% formamide, 6X SSC, 5X Denhardt's for 24 hrs. The filters were then washed in 1X SSC at 65C for 5 hrs and exposed to film for 3 days. Autoradiograms of the results are shown for the intron B (I) and exon 8 (II) probes. The intron B probe strongly hybridizes to bands representing the factor VII locus (1), (bands marked by dots) and cross-hybridizes with a number of sequences, including strong interactions (arrows) with other loci. The exon 8 probe hybridizes strongly only to fragments from the factor VII locus (dots) and weakly cross-hybridizes to other sequences. (λ = lambda HindIII digest)

Specific minisatellites are present as dispersed copies found throughout the genome. Some types of interspersed repetitive elements are related to one another through transposition of a common ancestor. In contrast, dispersed minisatellite copies are thought to have arisen independently and may share sequence similarities due to a common generation mechanism. This mechanism may involve sequences which serve as foci for recombination and give rise to the monomer core units of minisatellites. Dispersed minisatellite copies would be related through sharing similar originating foci (2). If this model is correct, it would be expected that MLEs composed of tandem repeats of monomers whose sequences have diverged greatly from their common core would be unlikely to cross react with other minisatellites, even those originating from similar foci. MLEs composed of monomers which faithfully adhere to their common core would be more likely to be able to hybridize to minisatellites which originated from similar foci. The contrast we observe between the exon 8 and intron B probes is consistent with this model.

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