A sequence polymorphism in the 3'-nontranslated region of the pro α 1 chain of type I procollagen

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Description, Source and Method: To date, only one RFLP (1) has been reported in the gene for the pro α 1(I) chain of type I procollagen (COL1A1).

cDNA and genomic DNA was PCR amplified with a 5' primer (5'-AGACCAGGAATTCGGCTTCG-3') spanning the EcoRI site in the pro α 1(I) C-propeptide and a 3' primer (5'-TTGGATCCAAGGTTGAATGCACTTTTGG-3') directed to nucleotides +203 to +222 (+1 being used to note the first nucleotide after the stop codon) and containing an additional BamHI site. Twenty-five cycles of amplification were performed at 94°C (1 min), 52°C (1 min), and 72°C (1 min) using a commercial kit (Cetus/Perkin-Elmer), and a DNA thermocycler. After digestion with EcoRI and BamHI, the 265 base pair fragment was cloned into M13 and sequenced.

The two alleles were distinguished by allele specific oligonucleotide hybridization (2). The oligonucleotide specific for the allele with a C had the sequence 5'-TGAACCCCCCAAAAGCCA-3' and the oligonucleotide specific for the allele with a T had the sequence 5'-TGGCTTTTGAGGGGGTTCA-3'.

Polymorphism: The sequence polymorphism was at position +88 (+1 being used to note the first nucleotide after the stop codon) of the pro α 1(I) chain mRNA. The nucleotide at +88 was either a C or a T (Fig. 1).

Frequency: Unrelated individuals studied: chromosomes from seven individuals of one family, from three individuals of another family, and from eight unrelated individuals were studied.

Five individuals were heterozygotes for either allele, eleven were homozygote for a T and two homozygotes for a C at position +88.

Mendelian Inheritance: The T and C sequence polymorphism was shown to be inherited in Mendelian manner in 7 individuals from 3 generations of one family and in 3 individuals from two generations of another family.

References: 1) Sykes, B. *et al.* (1986) *Lancet* **2**, 69–72. 2) Ijuta, S. *et al.* (1987) *Nucl. Acids Res.* **15**, 797–811.

A KpnI DNA polymorphism in the human von Willebrand factor (VWF) gene

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Source/Description: A 2.8 kb FspI-SacI fragment isolated from the 8.8 kb cDNA inserted in pGem2.

Polymorphism: KpnI (GGTACC) identifies several invariant fragments and a single two allele polymorphism with fragments at either 4.0 kb (A1) or 9.0 kb (A2).

Frequency: Estimated in 40 Caucasian North American chromosomes:

4.0 kb (A1): 0.56

9.0 kb (A2): 0.44

Not Polymorphic For: BglII, EcoRI, SacI, TaqI.

Chromosomal Localization: 12p12–12pter (Ginsburg *et al.*, 1985).

Mendelian Inheritance: Co-dominant segregation shown in 4 families.

Probe Availability: Probe available without restriction from Dr. D.C.Lynch.

Other Comments: Probe cross hybridizes with pseudogene sequence on chromosome 22 (Shelton-Inloes *et al.*, 1987). KpnI site localized to vWF sequence by HindIII/KpnI and SacI/KpnI digests of DNA from homozygous individuals. KpnI (+) sites cleave fragments localized to vWF gene sequence (*in figure).

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References: 1) Lynch *et al.* (1985) *Cell* **41**, 49. 2) Ginsburg *et al.* (1985) *Science* **228**, 1405. 3) Shelton-Inloes *et al.* (1987) *J. Clin.*