A deletion polymorphism in the human alpha-2-macroglobulin (A2M) gene

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Description: Alpha-2-macroglobulin is a major proteinase inhibitor in man. To study the bait domain, which defines the inhibitory spectrum of the protein and which is encoded by two exons (1), primers were designed to amplify the second exon. A 326 bp fragment was amplified by PCR using the intronic primers 5'-biotin-CTTTCCTTGATGACCCAAGCGCC-3' and 5'-GTTGAAAATAGTCAGCGACCTC-3'. 100 μ l containing 1 μ g human genomic DNA, 20 pmole of each primer, 200 μ M dNTPs in 50 mM KCl, 10 mM Tris-HCl (pH 8.3), 2 mM $MgCl_2$, 0.01% gelatin and 2U *Taq* polymerase (30 cycles of PCR: 1 min at 94°C, 40 s at 59°C, 40 s at 72°C).

Polymorphism: The sequence data showed a deletion of 5 bases from -7 to -3 from the 5' splice site of the exon.

Other Comments: The deletion is also detected by heteroduplex formation on non-denaturing PAGE. We have previously reported that the α 2-macroglobulin cDNA cross-hybridizes with the pregnancy zone protein gene (2). For this reason the reported RFLPs for the α 2M gene [David *et al.*, *Nucleic Acids Res.* **15** (1987) 374; Marynen *et al.*, *Nucleic Acids Res.* **13** (1985) 8287; Scambler *et al.*, *Nucleic Acids Res.* **13** (1985) 6787] should be reevaluated.

Chromosomal Location: 12p13.3-p12.3 (2).

Mendelian Inheritance: Codominant segregation was shown in 2 informative families.

Frequency: Frequencies of the two alleles among 132 unrelated Europeans and Mediterraneans:

TTCCTCACTCACCATAG/AGTCAGATGTA	p = 0.82
TTCCTCACTC---AG/AGTCAGATGTA	q = 0.18

(- deleted base; / consensus splice site)

References: 1) Marynen *et al.* (1990) *FEBS Letters* **262**, 349-352. 2) Devriendt *et al.* (1989) *Gene* **81**, 325-334.

Figure 1. Lane A shows the result for a mixture of PCR products from two individuals homozygous for the normal and the deletion allele (2.5 μ l each); lane B, from a heterozygous individual; lane C, from an individual homozygous for the deletion and lane D, from a normal homozygous individual. An arrow indicates the heteroduplex.

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