SSCP-polymorphism in intron 12 of the CFTR gene recognized by BclI

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Source/Description: SSCP analysis of intron 12 of the CFTR gene from PCR products showed an extra band in several DNA samples. Sequencing of the additional fragment extra band revealed a T→A change in the position 1898 + 152 of CFTR (Fig. 1). The change is a polymorphism which can be identified by SSCP or by BclI digestion.

Primer Sequences: Intronic primers described by Zielenski (1).
12i-5 5'-GTGAATCGATGTGGTGACCA-3'
12I-3 5'-CCTGGTTTAGCATGAGGCGGT-3'

Polymorphism: BclI digestion of the 426 bp PCR product separated on a 2% agarose gel identifies two-alleles: (A1) 426 bp, and (A2) 358 + 68 bp (Fig. 2).

Frequency: Estimated frequency for 30 normal chromosomes, 36 deltaF508 chromosomes and 32 non-deltaF508 CF chromosomes from Caucasoid individuals.

	Normals	CF-deltaF508	CF non-deltaF508 haplotype D	halplotypes A, B, C
A1	0.83	1.00	0.46	0.68
A2	0.17	0.00	0.54	0.32

Mendelian Inheritance: Autosomal co-dominant segregation was observed in 15 unrelated Spanish families.

Chromosomal Localization: CFTR has been localised to 7q31 (2).

Other Comments: The PCR reaction was performed on 250 ng of genomic DNA using 50 pmoles of each primer, 200 μM each dNTP and 1 unit of Taq polymerase. The amplification consisted of 35 cycles of 30 sec at 95°C, 40 sec at 56°C and 50 sec at 74°C. This polymorphism is useful as an intragenic marker for carrier screening and prenatal diagnosis of cystic fibrosis.

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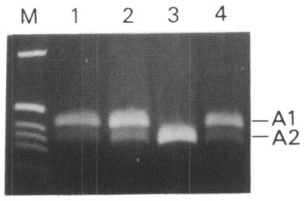
References: 1) Zielenski,J. *et al.* (1991) *Genomics* **10**, 214–228. 2) Rommens,J. *et al.* (1989) *Science* **245**, 1059–1065.



A *TaqI* RFLP in the N-terminal part of the gene for desmocollins DGII/III (psc)

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Source/Description: pJA2D6 contains a 1.8 kb *Eco*RI/*Xho*II fragment from the human desmocollins DGII cDNA out of a human keratinocyte library (1). DGII and DGIII molecules are generated by alternative splicing in the C-terminal region of the gene further downstream of this probe.

Polymorphism: *Taq*I digestion of genomic DNA and hybridization with the probe detects a two-allele polymorphism: 7.2 kb (A1) and 6.1 (A2).

Frequency: Estimated from 27 unrelated Caucasians
A1: 0.185,
A2: 0.815

Frequency of Heterozygosity: 0.30

Not Polymorphic For: *Eco*RI, *Bam*HI, *Bgl*II, *Pst*I.

Chromosomal Localization: Using a somatic cell hybrid panel the probe was assigned to chromosome 9p (2).

Mendelian Inheritance: Mendelian inheritance has been demonstrated in a three-generation family of the Utah kindred.

Probe Availability: Available for collaboration.

References: 1) Parker,A.E., Wheeler,G.N., Arnemann,J., Pidsley,S.C., Ataliotis,P., Thomas,C., Rees,D., Magee,Al., Buxton,R.S: (1991) Desmosomal glycoproteins II and III: Cadherin-like junctional molecules generated by alternative splicing *J. Biol. Chem.* **266**, 10438–10445. 2) Arnemann,J., Spurr,N.K., Wheeler,G.N., Parker,A.E., Buxton,R.S. (1991) Chromosomal assignment of the human genes coding for the major proteins of the desmosome junction, desmoglein DGI (DSG), desmocollins DGII/III (DSC), desmoplakins DPI/II (DSP), and plakoglobin DPII (JUP) *Genomics* **10**, 640–645.