Human LDL receptor gene: two ApaLI RFLPs

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SOURCE/DESCRIPTION: pLDLR3 contains a full-length LDL receptor cDNA (1). The vector is pcD minus the SV40 early region promoter. ApaLI is supplied by New England Biolabs. Its recognition sequence is GTGCAC.

POLYMORPHISM: ApaLI digestion generates a 3 allele polymorphism (Fig. 1). When a double digestion is carried out with BamHI, which is nonpolymorphic, four fragments are generated. There are two ApaLI polymorphic sites, one in intron 15 (ApaLI/I15) and one in the 3' flanking region (ApaLI/3') (2). 1) The ApaLI/I15 bi-allelic polymorphism identified by double digestion with BamHI generates two bands of 9.4 and 6.6 kb (Fig. 2) using an exon 16 and 17 specific probe generated from pLDLR3; 2) The ApaLI/3' bi-allelic polymorphism elucidated by codigestion with BamHI and a 3' exon 18 probe derived from pLDLR3, results in fragments of 17 and 13 kb in length (Fig. 3).

FREQUENCY: In 13 American Caucasian individuals:

ApaLI/I15:	9.4 kb	.58	ApaLI/3':	17 kb	.39
	6.6 kb	.42		13 kb	.61

CHROMOSOMAL LOCALIZATION: 19p13.1-13.3 (ref. 3)

MENDELIAN INHERITANCE: Co-dominant segregation demonstrated in 2 families (one shown in Fig. 2).

PROBE AVAILABILITY: pLDLR3 is available from the American Type Culture Collection, 12301 Parklawn Drive, Rockville, MD, 20852. Request strain number 57004.

COMMENTS: There appear to be only 3 alleles as the ApaLI/I15 polymorphism is in linkage disequilibrium with the ApaLI/3' polymorphism. We have screened 50 alleles and never see the presence of the ApaLI/I15 site in the absence of the ApaLI/3' site.

REFERENCES: 1) Yamamoto, T., et al. (1984) Cell 39: 27-38. 2) Südhof, T.C., et al. (1985) Science 228: 815-822. 3) Lindgren, V., et al. (1985) Proc. Natl. Acad. Sci. USA 82: 8567-8571.

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