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THE APOLIPOPROTEIN E POLYMORPHISM AT THE DNA-LEVEL

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Three different E2 mutants are known: E2 (ARG 145 → CYS), E2 (LYS 146 → GLN) and E2 (ARG 158 → CYS). These E2 mutants cannot be distinguished from each other by isoelectric focusing. The detection of apo E2 (ARG 158 → CYS) and apo E2 (LYS 146 → GLN) with synthetic oligomer-DNA probes will be presented. DNA fragments of nineteen basepairs, homologous to the mutated site (E2) or to the wild type (E3) are hybridized to human DNA. The conditions are chosen in such a way that only the perfect complementary DNA will hybridize. Using an apoE cDNA clone as hybridization probe a Restriction Fragment Length Polymorphism (RFLP) was detected with the restriction enzyme Hpal in both type III HLP patients and a control population. The digestion with Hpal leads to the finding of two discrete bands of 20 kb(H2) and 27 kb(H1) respectively. The two alleles H1 and H2 segregate in a Mendelian fashion. The H1 frequency is highest in controls (0.63 vs 0.37) whereas the H2 frequency is highest among the clinically diagnosed type III HLP patients (0.94 vs 0.06). Considering the apo E phenotype of the patients an association between the apoE phenotype and Hpal genotype is demonstrated. At present our findings suggest that homozygosity for the H2 allele is in the vast majority of cases (94%) indicative for the E2/2 phenotype.

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