TaqMan assays for genotyping of single nucleotide polymorphisms present at a disease susceptibility locus on chromosome 6.

Abstract:
Multiple single-nucleotide polymorphisms in the BAT1-NFKBIL1-LTA region on the short arm of chromosome 6 have been found to be associated with susceptibility to myocardial infarction in a recent case-control study including individuals from Japan. Specifically, the association relates to homozygosity for the minor alleles of five individual polymorphisms (one each in BAT1 and NFKBIL1 and three in LTA) and a haplotype defined by a particular allele combination of 10 polymorphisms (three each in BAT1 and NFKBIL1 and four in LTA). In the Japanese study, genotype determinations were carried out using a multiplex PCR-Invader assay or DNA sequencing. As an alternative to these methods, we have established TaqMan assays for genotyping of nine of the 10 polymorphisms. Accuracy of the genotyping results obtained with the TaqMan reactions was demonstrated in experiments involving restriction enzyme analysis or DNA sequencing. Using the new TaqMan assays, we have genotyped the polymorphisms in a group of 1211 Caucasians who presented without symptoms or signs of acute or previous myocardial infarction. Genotype distributions of each of the five myocardial infarction-associated polymorphisms were significantly different between the present study group and two Japanese control groups (p< or = 0.01). High linkage
disequilibrium measures between polymorphisms suggested that the nine polymorphisms reside in a single haplotype block. Based on the nine polymorphisms, eight different haplotypes with allele frequencies above 1% were identified, which together represented 98.4% of the total number of chromosome 6 in the 1211 individuals. This Caucasian study group and the Japanese sample showed strong linkage disequilibrium in the myocardial infarction-associated BAT1-NFKBIL1-LTA genomic region and related haplotype content, but significantly different genotype frequencies. The new TaqMan systems provide relatively simple and fast assays to test the clinical relevance of these polymorphisms.