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A Large Structural Rearrangement in the LDL Receptor Gene Causing Familial Hypercholesterolemia

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Familial hypercholesterolemia (FH) is a common autosomal dominant disorder caused by a defect in the low-density-lipoprotein (LDL) receptor, disrupting the normal control of cholesterol metabolism. Fourty-two unrelated heterozygotes for FH were screened to detect structural rearrangements in the LDL receptor gene. Genomic DNA was analyzed by Southern blot hybridization to probes encompassing exons 1-18 of the LDL receptor gene to detect large structural rearrangements. A novel deletion mutaion was detected in a FH pedigree. Southern blot analysis using the exon-specific probes revealed that this mutation elimianted exons 9, 10, 11, and 12. Detailed restriction mapping and sequence analysis mediated long-PCR demonstrated that this mutation was 5.72-kb deletion extending from intron 8 to 12, and has occurred between two *Alu*-repetitive sequences that are in the same orientation, one in intron 8 and the other in intron 12. We suggest that in this patient the deletion is caused by an unequal crossing-over event that occured between two homologous chromosomes at meiosis.

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Genetic Variations of the Apolipoprotein Genes in Koreans

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The apolipoprotein (apo) genes are candidates for determining lipid levels because their products are known to be involved in the transport and metabolism of lipid. In the present study, we investigated whether the particular RFLP of the apoAI-CIII-AIV cluster and apo(a) genes is associated with coronary artery disease (CAD). The allele frequencies of the *Hpa*II RFLP in the cluster gene were significantly different between male subgroups in the normal and CAD groups ($P<0.05$). The linkage disequilibrium was detected between pairs of RFLPs in CAD and normal groups, respectively. The frequency of the *Sst*I rare allele in our data was quite different from that in many other populations. Lipoprotein (a) levels were also significant differences among the apo(a) genotypes ($P<0.05$). Thus, these RFLP loci may provide the useful genetic information for clinical or population studies.