家族性高脂血症のアポ蛋白BおよびEの遺伝子DNAに関する研究

1986 Fiscal Year Final Research Report Summary

Studies on apolipoprotein B and E genes in familial hyperlipidemias

Research Project

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59480198

Research Category

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Allocation Type

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Research Field

内科学一般

Research Institution

University of Kanazawa

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Apolipoprotein E gene / Apolipoprotein E deficiency / Familial hypercholesterolemia / LDL receptor / LDL receptor gene / FH-Tonami / 遺伝子診断

Research Abstract

To probe a human adult liver cDNA library for apo-E cDNA clones, an oligonucleotide corresponding to apo E amino acids 218 to 222 was synthesized. One of 8 apoE cDNA clone (pAPOE7) was used as an apo E DNA probe for study of genomic DNA from a patient with apo E deficiency. Five micrograms of genomic DNA of apo E deficiency patient digested with Hind III or EcoRI, produced hybridization bands of approximately 1.9 and 12 Kb, respectively. The sizes of the hybridization bands were the same for normal controls and the proband's DNA.
Full length cDNA (pLDLR-3) and partial cDNA (pLDLR-2HHI) for human LDL receptor (LDlR) were used as LDLR DNA probes for studying genomic DNA from patients with familial hypercholesterolemia (FH) and normal subjects. Restriction fragment length polymorphism (RFLP) study of LDLR by PvuII showed allele A (16.5kb and 3.5kb) and allele B (14.0kb, 3.5kb and 2.5kb). The frequencies of the RFLP were determined in 28 FH patients and 13 normal subjects. The frequencies o f allele A and B in FH and normal subjects were 0.08 and 0.13, and 0.72 and 0.08, respectively.
Two patients (K.Y. and S.O.) with FH showed an abnormal fragment pattern of LDLR gene. After digestions with various restriction enzymes, we considered

that these two patients had a common mutant LDLR allele that had a 6kb deletion, and the deletion encompassed an area near the 5' end of exon 15 up to the Hind III site in intron 15. The FH phenotype and the abnormal fragment of LDLR completely cosegregated in all the 11 members of the family of K.Y. In the family of S.O, S.O and her two daughters (M.T. and C.M.) with FH showed an abnormal gragment of LDLR gene. The serum cholesterol levels of M.T.'s baby was 78 mg/dl. On Southern blotting analysis, the baby revealed an abnormal 10.5kb fragment. On the other hand, C.M.'s baby was normocholesterolemic (51 mg/dl) and showed no abnormal LDLR gene and was diagnosed as normal subject. We designated the patients with this new mutant gene as "FH-Tonami".▲ Less

Research Products (11 results)

All | Other

All | Publications (11 results)

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