Apolipoprotein E3Basel : new insights into a highly conserved protein region

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BACKGROUND: Apolipoprotein E is important for the receptor-mediated uptake of triglyceride-rich lipoproteins. Mutations in the gene encoding apolipoprotein E may cause a reduced uptake of these lipoproteins. Particular apolipoprotein E mutations have been also found to be associated with nephrologic, neurologic, and even ophthalmologic diseases. Hence, a continuously expanding role in biology is being attributed to this protein. DESIGN: Randomly selected volunteers from of a large Swiss cohort were genotyped for the common apolipoprotein E isoforms (apolipoprotein E2, apolipoprotein E3, apolipoprotein E4). RESULTS: In one of the volunteers, a novel C-to-T mutation causing an alanine-to-valine substitution (A106V, designated apolipoprotein E3Basel) was discovered. Alanine at residue 106 is highly conserved between mammalian species and is located in the immediate vicinity of the 112C/R polymorphism (apolipoprotein E4). Recombinant apolipoprotein E3Basel, expressed in the baculovirus system, displayed no detectable reduction in its low density lipoprotein (LDL) receptor- and heparin-binding activities. Despite normal binding functions, apolipoprotein E3Basel might cause modifications in the lipoprotein pattern. In the index case, plasma triglycerides were elevated and in two further apolipoprotein E3Basel-carriers, cholesterol, phospholipid, apolipoprotein CIII levels, LDL-cholesterol/apoB-100- and VLDL-triglyceride/VLDL-cholesterol-ratios were higher compared with apolipoprotein E3Basel-noncarriers when pair-matched for age and gender. One of the four apolipoprotein E3Basel-carriers from the index family had a personal history of Alzheimer's disease. CONCLUSIONS: Alanine at amino acid position 106 is highly conserved but not crucial in the receptor-mediated uptake of lipoprotein particles. Nevertheless, amino acid position 106 might be involved in the apolipoprotein E-dependent regulation of the lipoprotein lipase that hydrolyzes triglycerides and in the development of Alzheimer's disease.
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