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A NOVEL POLYMORPHIC PURINE COMPLEX AT THE UPSTREAM REGION OF THE HUMAN CAVEOLIN-1 GENE AND RISK OF ALZHEIMER'S DISEASE

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Crucial interaction of caveolin-1 (CAV1) with beta- and gamma-secretases, and aberrant expression of the gene encoding this protein in Alzheimer's disease (AD) support a role for CAV1 in the pathophysiology of this disease.
We report a novel polymorphic purine complex stretching ~150 bp of genomic DNA at the 1.5 kb upstream region of the human CAV1 gene, alleles and genotypes of which are associated with sporadic late-onset AD. Extra-short alleles were observed in the case group that were absent in the control subjects. Increased homozygosity for haplotypes was also observed at this region in the Alzheimer's cases, for those alleles and allele lengths shared by the case and control groups [(c^2=30.75, df=1, p< .000, OR=4.54, CI 95% (2.56-8.3)]. This region contains GGAA and GAAA motifs, the consensus binding sites for the Ets and IRF family transcription factors, respectively, and is highly conserved in distantly-related non-human primates in respect with location and motif sequence. The effect of this complex sequence on the expression of CAV1, and the related mechanisms in the pathophysiology of AD remain to be clarified.

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