FUNCTIONAL REGULATION OF ALU ELEMENT OF ACE GENE IN NEURON CELL

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Alzheimer's disease (AD) is the most common form of degenerated dementia with the pathological findings, neurofibrillary tangle, beta-amyloid, and neuronal loss. ACE insertion/deletion (I/D) genotype and its protein activity have been implicated to be associated with AD (AD). However, whether the insertion sequence, Alu element, in the intron 16 of human ACE gene plays functional role remains to be defined. By fusing the human ACE promoter region into the backbone reporter vector pSEAP-Basic2, we generated the pACEpro (f)-SEAP-Bas vector. To examine the regulation of the Alu element on the ACE promoter activity, the I- and D-form fragment of the intron 16 were inserted before the ACE promoter sequence of the pACEpro (f)-SEAP-Bas vector. Using transient transfection and luciferase reporter assay, our results showed that the transcriptional activity was increased ~70% in the reporter vector with I form than D form fragment in SH-SY5Y cells. The present data first indicates that Alu sequence, one of mammalian short interspersed elements (SINEs), in the human ACE intron 16 shows regulatory function on the ACE promoter activity. This encouraging finding could bridge the decade elusive gap between the protein level of ACE found in AD patients and the association of ACE polymorphism (I/D) with AD. Further investigation is needed to clarify what transcriptional factors may involved in the regulation of Alu element on ACE expression and whether this regulation are affected by external stress stimulation and causes degenerated dementia.