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# Neuronal protection by a variant of GAPDH pseudogene P44 in AD

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## ABSTRACT

GAPDH is a conserved enzyme that binds diverse proteins, such as Siah during apoptotic nuclear translocation. There is one somatic GAPDH gene, but over 60 pseudogenes, the expression of which is nebulous. A single nucleotide polymorphism (SNP) in the GAPDHP44 pseudogene exhibits a beneficial allele in AD. The objective of this study was to examine the P44 gene and to propose a mechanism for the putative protein and its impact on AD. We examined the sequences in the putative coding region of the human GAPDHP44 gene and the upstream genetic elements using a bioinformatics approach. We compared the amino acid sequences of the putative gene product with that of the parent GAPDH protein. There is a TATA box 24 nt upstream from, and a Kozak sequence at, putative transcription and translation start sites, respecttively. The upstream region also has sequences (7 - 16 nt) paralogous to those in parent gene introns; one shows homology to a known enhancer element. The resulting protein would contain 139 aa due to a stop codon, roughly the same size as the dinucleotide domain (151 aa) of the parent protein. The SNP is in a region (residues 80 - 120) that binds to the protein GOSPEL. We propose that the beneficial SNP may cause a glutamine to glutamate substitution. NMDA-stmulated neurons undergo GAPDH nitrosylation, Siah translocation, but can be rescued by GOSPEL binding to GAPDH. Our model suggests that the putative P44 protein may regulate GAPDH-GOSPEL interaction and the beneficial SNP may ameliorate AD.

## KEYWORDS

GAPDH, Alzheimer ' s Disease; Pseudogene; GAPDHP44; SNP; Apoptotic Nuclear Translocation; Siah; GOSPEL

## Cite this paper

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