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Rare Intronic Variations in *TP73* Gene Found in Patients with Alzheimer's Disease

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ABSTRACT *TP73* gene encodes p73 transcription factor, crucial for neurogenesis and neuronal health maintenance. In aging brain, p73 haploinsufficiency increases deposition of tau aggregates, hallmark pathology of Alzheimer's disease. Thus, *TP73* gene can be an important candidate for studying Alzheimer's disease susceptibility. To explore the role of nucleotide variations in regulatory region of *TP73* on Alzheimer's disease, the region encompassing exon 2 of 80 Alzheimer's patients and 123 age-matched controls was sequenced. Prediction of functional impact of found variations were done by software like 'SpliceAid', '*mutation* t@sting' and 'RegRNA2.0'.Two rare variations rs5031052 (NG_017035.2: g.34771C>T) and rs141679680 (NG_017035.2:g.34875G>A) were found in Alzheimer's patients in only heterozygous condition with minor allelic frequencies 0.01875 and 0.0125 respectively, significantly higher than global MAF count (p value of z test 0.04 and 0.01 respectively), but totally absent in the control group. In silico analysis reveals the importance of these variations in splicing and microRNA binding. These variations not only introduce intronic spicing enhancer motif but also modulate splicing factor recruitment. Moreover, they regulate microRNA binding by creating or destroying miRNA binding site. Thus, the researchers report, for the first time that these two rare variations may involve in manifestation of Alzheimer's disease in our cohort.