In silico analysis of TREM2 gene involved in Alzheimer's disease

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Abstract: Alzheimer's disease (AD), the most prevalent neurodegenerative disorder, is described by slowly progressive cognitive decrease. The number of people affected by AD was 26.6 million worldwide in 2006. By 2050, however, the prevalence is expected to quadruple [1]. Neuroinflammation plays a pivotal role in the pathophysiology of neurocognitive disorders such as AD. Multiple studies have found that heterozygous carriers of rare variants within the TREM2 gene increase the risk of developing late-onset AD [2]. At the present study, to investigate evolutionary relationship of *TREM2* in human compared to other organisms, ClustalX, GENEDOC and Treeview softwares and for investigation of gene network and matrix families throughout the promoter region of *TREM2* gene, GeneMANIA and Gene2promoter softwares were used, respectively [3]. Regarding to phylogenetic tree achieved by analysis of *TREM2* nucleotide sequence, *Homo sapiens* has the highest and lowest similarity to *Nomascus leucogenys* and *Hipposideros armiger*, respectively. Altogether, sequence analysis of this gene showed its highly conserved sequence. Furthermore, study of gene network related to *TREM2* showed its physical interaction with TYROBP, as tyrosine kinase and putative receptor for *TREM2* so that its disturbance might contribute to early-onset AD risk. Analysis of *TREM2* gene promoter showed the the presence of 13 matrix families ($P<0.05$). Among the key matrix families can be point out to SORY that is family of SOX/SRY and related HMG box factors (The Sox family presents an intriguing instance of highly conserved DBDs with closely related but distinct binding preferences) and ETSF (promoter region specific for protein transporters and effective in T cell activation) and RXRF (retinoid X receptor gamma that increases both DNA binding and transcriptional function on its respective response elements causing the decline of amyloid-beta) [4]. Overall, understanding the role of TREM2 and microgliosis in AD may help to treatment of the disease, which could ultimately lead to novel drug targets to delay or prevent the progression to clinical dementia.

Key words: Alzheimer; TREM2; Phylogenetic; Gene network; Promoter

References:

[1] W. A. Rocca, R. C. Petersen, et al. "Trends in the incidence and prevalence of Alzheimer's disease, dementia, and cognitive impairment in the United States". 7(1) (2011) 80-93.

[2] JD.Ulrich, DM .Holtzman. "TREM2 function in Alzheimer's disease and neurodegeneration", J. ACS chemical neuroscience. 7(4) (2016) 420-7.

[3] P. Pooya, F. Parvini, "In silico analysis of GJB2: A key gene causing non-syndromic hearing loss". The Second International & Fourteenth Iranian Genetics Congress, Tehran, Iran. (2016)

[4] G. Badis, M.F. Berger, A.A. Philippakis, S.Talukder, et al. "Diversity and complexity in DNA recognition by transcription factors." J. Science., 5935 (2009) 1720-1723.