ATM, a new therapeutic target in the treatment of epilepsy

Maryam Rahimi-Tesiye
Shahid Beheshti University, University, Iran

Introduction: Epilepsy, one of the most common neurological disorders, is associated with reversible seizures, indicating the abnormality of the brain circuits. Different genetic and environmental factors as well as brain tumors are involved in the development of the disease. However, its molecular mechanism is not well understood [1]. In this study, changes in the microenvironment around brain tumors and changes in gene expression of astrocytes, which are involved in epileptogenesis, have been investigated.

Method: The samples with GSE32534 were downloaded from the GO database, then R package "limma" was applied to determine DEGs. Using the Log2FC criterion, -4.362≤ Log2FC ≤ -2.000 and P-value <0.05, 709 highly under-expressed genes were selected and entered into the STRING database for PPI analysis. The network was then rebuilt in Cytoscape software and finally, 99 hub genes with a high score of degree, betweenness and closeness centrality were selected. Enrichment analysis of these hub genes was performed in Gaphi software to determine the modules.

Results and discussion: Hub genes with the highest scores were mainly involved in biological processes such as cell division, neuronal differentiation, migration, regulation of neurotransmitters, etc. Based on the analysis ATM gene, encodes a serine/threonine kinase and activates P53 in response to DNA double-strand breaks, [2] received the highest score considering all three parameters. ATM is involved in neurological processes such as neuronal survival, proliferation, and synaptic vesicle recycling [3,4] play key role in regulating neurotransmission and the proper functioning of neurons, and many anticonvulsant drugs target such functions [5]. Enrichment analysis revealed the network formed by ATM is mainly involved in glioblastoma signaling pathways, DNA IR- double strand breaks, P53 signaling, and cell cycle.

Conclusion: It can be concluded that down-regulation of ATM through triggering the above pathways can induce epileptogenesis and its targeting can be a new therapeutic goal.

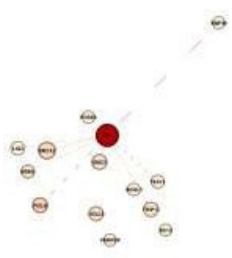

Figure 1: protein-protein network interaction of ATM

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Biography

Maryam Rahimi-Tesiye working as Faculty of Life Science and Biotechnology at Shahid Beheshti University, Tehran, Iran.

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