MiR-107 Activates NF-κB versus Aβ Analysis of the regulatory effect of 1-42 induced apoptosis in Alzheimer's disease cells

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ABSTRACT

Alzheimer's disease (AD) is one of the acute degenerative diseases of the brain that occurs in the central nervous system. This disease is caused by the abnormal deposition of insoluble plaques and peptide amyloid beta (Aβ), the formation of nodules, and synaptic disorder. The formation of these nodes disrupts the functioning of neural circuits and changes in behavioral response due to the activation of neurotransmitter receptors. Research in recent years has shown that microRNAs play an effective role in Alzheimer's disease and neurotransmitter factors. Recently, miR-107 is effective in the pathology of Alzheimer's disease (AD) through the regulation of the NF-κB signaling pathway. Experiments conducted using the dual luciferase method and western blot analysis also showed that miR-107 in primary neurons affects neurotransmitter factors in Alzheimer's patients. On the other hand, increasing the expression of miR-107 leads to increasing the breaking process of Amyloid precursor protein (APP). This factor increases the production of amyloid beta (Aβ) peptide plaques and increases the expression of the BACE1 gene, which ultimately leads to the induction of apoptosis and induction of Alzheimer's disease.

Materials and Methods

First, the sequence of MiR-107 (Accession number:

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MI0000114) was obtained from the NCBI database. Then the exact location of this microRNA was determined using the UCSC database, then the ProtScale database was used to obtain the molecular weight and isoelectric point of MiR-107. Cell comparison and analysis of genes effective in microRNAs were analyzed by the Human Protein Atlas OMIM database. Finally, the Alliance of Genome Resources database was used to investigate the expression of MiR-107 in different body organs and western blot analysis.

Results

MiR-107 is one of the most important types of microRNAs that play an important role in the induction of apoptosis and Alzheimer's disease. Table 2 shows the specific characteristics of this microRNA along with molecular weight and isoelectric point (31).

BACE1 encodes a gene from the peptidase A1 family of aspartic proteases. This protease catalyzes the first step in the formation of the beta-amyloid peptide from the amyloid precursor protein. Beta-amyloid peptides are the main component of beta-amyloid plaques that accumulate in the brains of human Alzheimer's patients (32). The MIR107 factor leads to an increase in the expression of this gene through the NF-κB signaling pathway and breaking APP Amyloid precursor protein. Also, the inflammatory mechanisms of the NF-κB signaling pathway in the brain are activated in response to Aβ plaques. Several reports indicate that T cells are also activated in patients with AD and that these cells are present both in the environment and infiltration in the brain. Also, inhibiting the NF-κB-related SYK signaling pathway suppresses cell apoptosis through the reduction of MIR107 expression (33). The schematic Figure 1 shows the effect of MIR107 on the amyloid genetic pathways.

Table 1. The name and role of the main genes involved in the pathogenesis of Alzheimer's disease and the microRNAs reported for these genes.

<table>
<thead>
<tr>
<th>Gene name</th>
<th>Related microRNAs</th>
<th>The role of target gene protein in Alzheimer's disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>APP</td>
<td>miR-200-b, miR-106a, miR-106b, miR-101, miR-17-5p, miR-153, miR-16, miR-101, miR-339-5p, miR-29a/b, miR-29c, miR-107, miR-298, miR-328, miR-195, miR-124, miR-135a, miR-135b, miR-186</td>
<td>Overexpression of amyloid-beta precursor protein causes more amyloid-beta production, and this process leads to neurotoxicity and synaptic disorder (12).</td>
</tr>
<tr>
<td>BACE1</td>
<td>miR-132</td>
<td>The process of breaking down APP and producing amyloid beta (Aβ) (13)</td>
</tr>
<tr>
<td>Tau</td>
<td>miR-132</td>
<td>Phosphorylation of tau (14)</td>
</tr>
<tr>
<td>Fyn</td>
<td>miR-106-b</td>
<td>Phosphorylation of tau (15)</td>
</tr>
<tr>
<td>PTPN1</td>
<td>miR-124</td>
<td>It plays a role in synaptic dysfunction and suppression of PTPN1 (16)</td>
</tr>
<tr>
<td>ITPKB</td>
<td>miR-132</td>
<td>It plays a role in the accumulation of amyloid beta (Aβ) (17)</td>
</tr>
<tr>
<td>Sirt1</td>
<td>miR-132</td>
<td>De-acetylating various protein targets has a protective effect against Alzheimer's disease (18)</td>
</tr>
<tr>
<td>NOS1</td>
<td>miR-132</td>
<td>It is involved in the pathway of tau phosphorylation (19)</td>
</tr>
<tr>
<td>PTEN</td>
<td>miR-132, miR-212</td>
<td>It plays a role in beta-amyloid neurotoxicity (20)</td>
</tr>
<tr>
<td>FOXO3</td>
<td>miR-132, miR-212</td>
<td>It plays a role in beta-amyloid neurotoxicity (20)</td>
</tr>
<tr>
<td>TNFAIP1</td>
<td>miR-137</td>
<td>Changes in BDNF expression in specific neuronal subtypes (22)</td>
</tr>
<tr>
<td>BDNF</td>
<td>miR-10a</td>
<td>Decreased synaptic functions (23)</td>
</tr>
<tr>
<td>UCHL1</td>
<td>miR-922</td>
<td>Phosphorylation of tau (24)</td>
</tr>
<tr>
<td>RARA</td>
<td>miR-138</td>
<td>Increase of Aβ42, Aβ40 (25)</td>
</tr>
<tr>
<td>SNX6</td>
<td>miR-98-5p</td>
<td>Phosphorylation of tau (26)</td>
</tr>
<tr>
<td>ROCK1</td>
<td>miR-146a</td>
<td>Decreased synaptic functions (27)</td>
</tr>
<tr>
<td>VAMP2</td>
<td>miR-34C</td>
<td>Abnormal phagocytosis (28)</td>
</tr>
<tr>
<td>SPHK1</td>
<td>miR-125b</td>
<td>Decrease of Aβ42, Aβ40 (25)</td>
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<tr>
<td>VAV1</td>
<td>miR-330</td>
<td>Oxidative stress and mitochondrial dysfunction (29)</td>
</tr>
<tr>
<td>ApoE</td>
<td>miR-1908</td>
<td>Reduction of amyloid beta (Aβ) accumulation (30)</td>
</tr>
</tbody>
</table>

Nuclear factor-kB (NF-kB)

Nuclear factor NF-kB is a family of transcription fac-
tors that plays an important role in inflammation, immunity, cell proliferation, differentiation, and survival. NF-κB activation depends on proteasome degradation caused by inhibitory phosphorylation. NF-κB acts as a central mediator of the immune and inflammatory systems and plays a role in stress response and regulation of cell proliferation and apoptosis. In general, the corresponding NF-κB target genes allow organisms to effectively respond to these environmental changes. Most effects of the NF-κB signaling pathway are related to the induction of kinase and phosphorylation. In this pathway, protein kinase inhibitors IkBs play an important role and the combination of these factors ultimately leads to the activation of dimers such as p52-ReIB. (MIR107) microRNA 107 is one of the types of microRNAs that affect the NF-κB signaling pathway through phosphorylation (Figure 2) (34). In the last two decades, tremendous progress has been made in discovering the details that have made it possible to understand the general principles of signal transduction and gene regulation.

**Examination of MiR-107 expression**

The analysis of gene expression in the anatomy of *Mus musculus* and *Homo sapiens* showed that the expression level of MiR-107 is higher in the nervous system, respiratory system, vestibule-auditory system, Mesenchyme, ectoderm, Appendage, pharyngeal arch, entire extra embryonic component, and sensory system and is seen in all stages, especially in the embryo stage and post-juvenile adult stage (Figure 3).

**Western blot analysis**

Figure 4 shows a Western blot analysis of BACE-1 in human brain tissue (Alzheimer’s disease hippocampus). PVDF Membrane was probed with 2 µg/mL of Mouse Anti-Human/Mouse BACE-1 Ectodomain Monoclonal Antibody (Catalog MAB931) followed by HRP-conjugated Anti-Mouse IgG Secondary Antibody (Catalog HAF007). The resulting Specific bands for BACE-1 were detected at around 60 and 70 kDa (as indicated) (Figure 4). This test was performed under reducing conditions and using the Immunoblot buffer in Table 3.

**Discussion**

Currently, 850,000 people in the UK are suffering from Alzheimer’s disease, which is expected to increase to 1.1 million people by 2025 due to the increasing trend of this disease and its rapid progress. Alzheimer’s disease
Conclusion

Reduces miR-107 expression by regulating NF-κB signaling pathway, thereby inhibiting apoptosis in Alzheimer's disease patients. On the other hand, increased expression of miR-107 leads to increased fragmentation of amyloid precursor protein (APP). This factor increases the production of amyloid (Aβ) peptide plaques and increases the expression of the BACE1 gene, ultimately leading to the induction of apoptosis and the induction of Alzheimer's disease.

Conflicts of interests

The authors state no conflicts of interest in this study.

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References

10. Alsaeidy, H. K., Mirzaei, A. R., and Alhashimi, R. A. H. Investigating the structure and function of Long
Non-Coding RNA (LncRNA) and its role in cancer. CMBR.2022; 2(4), 245-253.
31. Mirzaei, A. R., and Fazeli, F. Bioinformatics analysis of microtubule-associated protein-1 light chain 3 (MAP1LC3A) and (BECN1) genes in autophagy. CMBR. 2022; 2(3), 129-137.
34. Oechinghaus, A., and Ghosh, S. B Family of Transcription Factors and Its Regulation. The NF.