EDITORIAL

Therapeutic targeting of mirnas as potential therapy for alzheimer's disease

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DESCRIPTION

Alzheimer's disease has always been an unpleasant burden for many people aged over 85 or even less and it has been supposedly harder to encounter for the families of the patients and those around them. Considering both the agony and the costs dedicated for this disease, it has imposed a high morbidity rate to all societies. Alzheimer's disease is mainly caused by amyloid aggregation in the brain, mostly in the temporal and parietal lobes; and formation of neurofibrillary tangles which all lead to cortex atrophy and presentation of memory loss and failure in cognitive acts. The specific type of amyloid protein responsible for Alzheimer's disease progression is amyloid-beta, produced by the enzyme beta secretase. While the physiological role of this enzyme is still under debate, a decrease in its production may lead to a relative decrease in the severity of Alzheimer's disease presentations in a patient. MicroRNAs, on the other hand, are well-known types of RNAs which moderate gene expression. They may also be used as a therapeutic target to inhibit the expression of the gene responsible for beta secretase enzyme production and consequently decrease the unpleasant symptoms of Alzheimer's disease. In this review, possible therapeutic acts and aspects of Alzheimer's disease are explained, which may be considered for further research. Alzheimer's Disease (AD) is a progressive, age-dependent neurodegenerative disease characterized by the accumulation of β-amyloid plaques and hyper phosphorylation of tau proteins, which induce the development of neurofibrillary tangles, resulting in a gradual decrease in cognition and short-term memory. Patients show memory, judgment, orientation and language impairment, mood swings, and hallucination. Advanced age and family history are risk factors. Several genes have been linked with AD, including Amyloid-Beta Precursor Protein (APP), Collagen, type XXV alpha 1 chain (COL25A1), Bromo Domain PHD Finger Transcription Factor (BPTF) and Caspase2 (CASP2). Numerous studies have proposed that dysregulation of microRNAs impact on the pathophysiology of the disease; thus, they could represent a novel therapeutic approach to prevent or even stop AD progression. In 2015, conducted an experiment in which overexpression of miRNA-16 was achieved in mice brains through the delivery of oligonucleotide using an osmotic pump, resulting in down regulation of GfapanAif1, providing neuron protection and oxidative stress prevention, respectively while an in vitro experiment using cell transfection to up-regulate miR-16 ended up in a reduction of Tau phosphorylation, BACE1and APP genes. Likewise, in Neuro2a cells, reduction in tau protein expression was observed after being transfected with miR-132 mimics, which were later introduced in mice by osmotic pumps to enhance long-term memory. Similarly, intracerebro ventricular ICV injections containing oligonucleotides of miR-132 mimics were applied in mice; resulting in amplified levels of inositol 1,4,5-trisphosphate 3-kinase B (ITPKB), linked with tauphosphorylation and β-Amyloid Peptide (Aβ) deposition.

CONCLUSION

Analogously, it has been shown that overexpression of miR-124 via cell transfection in PC12cells (a cell line derived from a pheochromocytoma of the rat adrenal medulla) and primary culture of hippocampal neurons, prevent cell damage and lowerBACE1expression, which is involved in β-amyloid peptide production. Additionally, PC12 cells along with SH-SY5Y cells were transfected with miR-193a-3p mimics, inhibitor, and negative controls; the overexpression of the miRNA, which targets PTEN gene, was able to reduce neurotoxicity produced by β-Amyloid. Transfected PC12 cell with miR-107 while simultaneously subjecting them to 6-hydroxydopamine (6-OHDA), a neurotoxin known for inducing motor abnormality; results exhibited a decrease inCaspase-3 activity, a protein linked with apoptosis, along with repression in LDH release (that occurs after cell damage) and the elevation of SOD to reduce oxidative stress associated ROS activity. This study identified programmed cell death 10 (PDCD10) proteins as a target of miR-107. Moreover, in a consequent in vivo assay, tail vein injection of a recombinant lenti virus expressing miR-107 was applied to mice treated with 6-OHDA, resulting in the up-regulation of miR-107 and consequently repressing 6-OHDAeffects. The same delivery mechanism was used by other workers to introduce miR-326 lent viral vectors into mice, and after analysing the brain tissue, it was observed that overexpression of miR-326 was favourable, since it inhibited JNK signalling pathway, leading to an improvement of cognitive function; accumulation of Aβwas reduced andVAV1protein expression was restrained.

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