

miRNAs: Role of Post-Transcriptional Regulation of NLRP3 Inflammasomes in the Treatment of Neurodegenerative Disorders

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ABSTRACT

Role of inflammasomes is studied very well. They are multiprotein complexes consist of having nucleotide binding domain and leucine rich repeat with the pyrin and HIN domain family. The NLRP3 inflammasome one of these members of family. It is activated upon sensing microbes or danger associated molecular pattern. NLRP3 inflammasome activation leads to activation of caspase 1 which is in turn activate proinflammatory cytokines/chemokines.

The role of NLRP3 inflammasome in Alzheimer's disease has recently been identified. NLRP3 inflammasome activation is necessary for maturation of IL-1 β , IL-18 these cytokines/chemokines. Prolong activation of NLRP3 inflammasome and release of these cytokines/chemokines, along with neuronal cell death serve as danger signal to further excitation of NLRP3 activation in this way, neuronal cell death provides feedback loop and deteriorate the pathophysiological condition.

Deficiency or inhibition of NLRP3 inflammasome can be beneficial to reduce the deleterious effect of neuroinflammation in pathophysiology of AD. It has been described that NLRP3 inflammasome activity is under the control of additional transcriptional regulation.

This study identifies the role of microRNA such as miR-223 in the regulation of NLRP3 inflammasome. miR-223 is a critical regulator of NLRP3 inflammasome activity. miR-223 suppresses NLRP3 expression through a conserved binding site within the 3' untranslated region of NLRP3, translating to reduced NLRP3 inflammasome activity. It is interesting to note that miR-223 itself is not regulated by proinflammatory signals, its expression varies among different myeloid cell types. Therefore, given the tight transcriptional control of NLRP3 message itself, miR-223 functions as an important rheostat controlling NLRP3 inflammasome activity. Therefore, induction of therapeutic treatment target to NLRP3 inflammasome may be beneficial to neurodegenerative disease such as Alzheimer's disorder.

Keywords: Proinflammatory, NLRP3, Alzheimer's disorder

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