The potential role of miRNA therapies in spinal muscle atrophy

ABSTRACT

Spinal muscular atrophy (SMA) is a neurodegenerative disease caused by low levels of full-length survival motor neuron (SMN) protein due to the loss of the survival motor neuron 1 (SMN1) gene and inefficient splicing of the survival motor neuron 2 (SMN2) gene, which mostly affects alpha motor neurons of the lower spinal cord. Despite the U.S. Food and Drug Administration (FDA) approved SMN-dependent therapies including Nusinersen, Zolgensma® and Evrysdi™, SMA is still a devastating disease as these existing expensive drugs may not be sufficient and thus, remains a need for additional therapies. The involvement of microRNAs (miRNAs) in SMA is expanding because miRNAs are important mediators of gene expression as each miRNA could target a number of genes. Hence, miRNA-based therapy could be utilized in treating this genetic disorder. However, the delivery of miRNAs into the target cells remains an obstacle in SMA, as there is no effective delivery system to date. This review highlights the potential strategies for intracellular miRNA delivery into target cells and current challenges in miRNA delivery. Furthermore, we provide the future prospects of miRNA-based therapeutic strategies in SMA.

Keyword: Spinal muscular atrophy; MicroRNAs; miRNA-based therapy; miRNA delivery