Advanced Engineering Days

aed.mersin.edu.tr

Spinal Muscular Atrophy (SMA) and mRNA-based therapy against it

Simay Ayden [*1], **Furkan Ayaz** [1, 2]

[1]*Mersin University, Biotechnology Department, Türkiye, 21140940006@mersin.edu.tr*
[2]*Mersin University, Biotechnology Research and Application Center, Türkiye, furkanayaz@mersin.edu.tr*

Cite this study: Ayden, S., & Ayaz, F. (2022). Spinal Muscular Atrophy (SMA) and mRNA-based therapy against it. 4th Advanced Engineering Days, 4-5

Keywords
SMA
Treatment
SMN protein

Abstract

Spinal Muscular Atrophy (SMA), is a genetic disease caused by the loss of nerve cells called motor neurons. It occurs as a result of the inability to produce the SMN protein, which is a motor neuron protein. Currently, no treatment has been found for the complete recovery of people with SMA. However, the symptoms of the disease can be reduced through medications. The main problem, the inability to produce the SMN protein, can be achieved by using mRNA-based therapy. The mRNA-based therapy basically contains the code for the protein we want to be produced, and thus that protein is produced by the body. This is how the missing protein that causes SMA can be rescued.

Introduction

SMA is caused by the impairment of the special nerve cells that are called motor neurons which are in charge of the motor functions such as muscle movement [1]. SMA is a disease that occurs as a result of deletions in the SMN1 gene, The SMN1 gene cannot produce the SMN protein. The SMN2 gene is a paralog of the SMN1 gene. The SMN2 gene encodes the SMN protein, but most of it is non-functional. But it still helps reduce the severity of the disease in most SMA patients who have more copies of the SMN2 gene [2]. Loss of motor neurons affects the muscles involved in the control of the head, arm and leg movement. These impairments are evident in different types of SMA patients. There are 5 types of SMA types. It has in an autosomal recessive manner inheritance mechanism [3].

Results

SMA occurs in 1 out of every 10,000 births. Men and women are affected equally by the disease [2].

There are 5 types of SMA disease.

1. SMA 0: Symptoms are severe weakness and respiratory distress at birth. These infants have severe respiratory failure. Most babies rarely survive beyond 6 months.

2. SMA I: The mean age of onset of symptoms is 2.5 months. Symmetrical muscle weakness, regression of motor functions and lack of motor development, weak muscle tone are among the main symptoms. Most patients survived 24 months with supportive care.

3. SMA II: The mean age of onset of symptoms is 8.3 months. Weak muscle tone is evident at birth or in the first few months. It has symptoms such as developmental delay with impairment of motor skills, proximal muscle weakness, postural tremor of the fingers. 68% of patients are still alive at 25 years of age.

4. SMA III: Occurs after 18 months of age. It has symptoms such as proximal muscle weakness, loss of motor skills, and postural tremor of the fingers. Life expectancy is high for these patients.

5. SMA IV: Unlike other types, it appears with muscle weakness at the age of 20 or 30 years. Among its symptoms is fatigue. It is the least common type and does not affect life expectancy [4].

The SMN protein, consisting of 38 kDa and 294 amino acids, is encoded by 2 genes. However, mutations in the centromeric SMN (SMN(C)) of these genes cause SMA disease [5]. Today, many treatment methods are being developed. Small molecules, oligonucleotides and gene replacement have been attempted to increase SMN protein levels [6].

Discussion

mRNA (messenger RNA) produces protein according to the genetic code it carries. It is possible to fulfill the function of a single protein with protein replacement [7].

The deficiency of the SMN protein that causes SMA can be produced and its functional form can be rescued by the mRNA-based therapy.

References

1. MedlinePlus Genetics (2020). Spinal muscular atrophy
2. NORD (2019). Spinal Muscular Atrophy.
3. GARD (2019). Spinal muscular atrophy.
4. Prior, T. W., Leach, M. E., & Finanger, E. (2020). Spinal muscular atrophy. University of Washington, Seattle, Seattle (WA), PMID: 20301526
5. Coovert, D. D., Le, T. T., McAndrew, P. E., Strasswimmer, J., Crawford, T. O., Mendell, J. R., ... & Burghes, A. H. (1997). The survival motor neuron protein in spinal muscular atrophy. *Human molecular genetics*, *6*(8), 1205-1214.
6. Arnold, E. S., & Fischbeck, K. H. (2018). Spinal muscular atrophy. *Handbook of clinical neurology*, *148*, 591-601.
7. Kowalski, P. S., Rudra, A., Miao, L., & Anderson, D. G. (2019). Delivering the messenger: advances in technologies for therapeutic mRNA delivery. *Molecular Therapy*, *27*(4), 710-728.