From Gene to Syndrome: Understanding the Relationship Between Alternative Splicing in Elastin and ASD Development

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Alternative splicing is a process that occurs during gene expression, in which a gene codes for multiple proteins by including or excluding segments (exons) from the mRNA transcript. The spliceosome is a complex of proteins that plays a major part in alternative splicing process and is critical for the proteins' variety required in different cellular pathways. ASDs (Autistic Spectrum Disorders) are complex neurodevelopmental disorders that affect communication and behavior. A mutation in WBP4 gene, that codes for a spliceosome component, was found in a patient with low-functioning ASD diagnosis. This resulted in a defect in the alternative splicing of 2852 genes, including the over-inclusion of an exon in the ELN gene. The ELN gene codes for elastin– a structural protein responsible for the elasticity and flexibility of tissues. Elastin is a significant component of the myelin sheath in the brain, which is essential for brain connectivity. In order to understand the relationship between the damage to the spliceosome and the defective expression of the elastin protein, a normal WPB4 gene coupled with a GFP gene was inserted into cells extracted from the patient, in addition to a monitoring cell line with only GFP. Following extraction of RNA from the samples and synthesizing cDNA, a significant decrease in the amount of the defective ELN transcript, and an increase in the amount of the normal transcript were detected in real-time qPCR when compared to the patient's normal cells with only GFP. These results show that by inserting the normal gene of WBP4, we are able to increase the rate of the normal transcript of ELN in the patient's cells, which provides an innovative and more profound insight of ASD pathophysiology.

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