TARDBP Gene

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TAR DNA binding protein: The TARDBP gene provides instructions for making a protein called transactive response DNA binding protein 43 kDa (TDP-43).

Keywords: genes

1. Normal Function

The *TARDBP* gene provides instructions for making a protein called transactive response DNA binding protein 43 kDa (TDP-43). This protein is found within the cell nucleus in most tissues and is involved in many of the steps of protein production. The TDP-43 protein attaches (binds) to DNA and regulates an activity called transcription, which is the first step in the production of proteins from genes. This protein can also bind to RNA, a chemical cousin of DNA, to ensure the RNA's stability. The TDP-43 protein is involved in processing molecules called messenger RNA (mRNA), which serve as the genetic blueprints for making proteins. By cutting and rearranging mRNA molecules in different ways, the TDP-43 protein controls the production of different versions of certain proteins. This process is known as alternative splicing. The TDP-43 protein can influence various functions of a cell by regulating protein production.

The *TARDBP* gene is particularly active (expressed) during early development before birth when new tissues are forming. Many of the proteins whose production is influenced by the TDP-43 protein are involved in nervous system and organ development.

2. Health Conditions Related to Genetic Changes

2.1. Amyotrophic lateral sclerosis

At least 60 mutations in the *TARDBP* gene have been found to cause amyotrophic lateral sclerosis (ALS), a condition characterized by progressive muscle weakness, a loss of muscle mass, and an inability to control movement. Most mutations change single protein building blocks (amino acids) in the TDP-43 protein. The majority of these changes affect the region of the protein involved in mRNA processing, likely disrupting the production of other proteins. Changes to the TDP-43 protein cause the protein to misfold and form protein clumps (aggregates), which have been found in nerve cells that control muscle movement (motor neurons) in some people with ALS. It is unclear whether TDP-43 protein aggregates causes the nerve cell death that leads to ALS or if they are a byproduct of a dying cell.

Some people with ALS caused by *TARDBP* gene mutations also develop a condition called frontotemporal dementia (FTD), which is a progressive brain disorder that affects personality, behavior, and language. It is unclear why some people with *TARDBP* gene mutations develop FTD and others do not. Individuals who develop both conditions are diagnosed as having ALS-FTD.

2.2. Other disorders

Mutations in the *TARDBP* gene have been found to cause frontotemporal dementia (FTD) without features of amyotrophic lateral sclerosis (ALS, described above). FTD caused by *TARDBP* gene mutations is characterized by a gradual loss of problem-solving skills and language comprehension. Affected individuals often have changes in personality and behavior that may make it difficult to interact with others in a socially appropriate manner. Most *TARDBP* gene mutations that cause FTD change single amino acids in the TDP-43 protein. These mutations are thought to affect only part of the protein, leaving other parts of the protein functional. Because these *TARDBP* gene mutations result in a protein with some residual function, the features of the condition tend to appear later in life, in one's late sixties or early seventies. Some people who inherit the altered *TARDBP* gene never develop FTD, a situation known as reduced penetrance.

3. Other Names for This Gene

- ALS10
- TADBP_HUMAN
- TAR DNA-binding protein 43
- TAR DNA-binding protein-43
- TDP-43

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