ATXN3 gene

ataxin 3

Normal Function

The ATXN3 gene provides instructions for making an enzyme called ataxin-3, which is found in cells throughout the body. Ataxin-3 is involved in a mechanism called the ubiquitin-proteasome system that destroys and gets rid of excess or damaged proteins. The molecule ubiquitin attaches (binds) to unneeded proteins and tags them to be broken down (degraded) within cells. Ataxin-3 removes (cleaves) the ubiquitin from these unwanted proteins just before they are degraded so that the ubiquitin can be used again. Due to its role in cleaving ubiquitin from proteins, ataxin-3 is known as a deubiquitinating enzyme.

Researchers believe that ataxin-3 also may be involved in regulating the first stage of protein production (transcription).

Health Conditions Related to Genetic Changes

Spinocerebellar ataxia type 3

Spinocerebellar ataxia type 3 (SCA3) is a condition characterized by progressive problems with movement. SCA3 results from a mutation in the *ATXN3* gene known as a trinucleotide repeat expansion. This mutation increases the length of the repeated CAG segment in the *ATXN3* gene. People with SCA3 have more than 50 CAG repeats.

The expanded CAG segment leads to the production of an abnormally long version of the ataxin-3 protein that folds into the wrong 3-dimensional shape. This nonfunctional ataxin-3 protein cannot remove ubiquitin from proteins that are no longer needed. As a result, these unwanted proteins, along with ubiquitin and ataxin-3, cluster together to form clumps (aggregates) within the nucleus of the cells. It is unclear how these aggregates affect cell function, because they are found in healthy cells as well as those that die.

Nerve cells (neurons) and other types of brain cells are most affected by mutations in the *ATXN3* gene. SCA3 is associated with cell death in the part of the brain that is connected to the spinal cord (the brainstem), the part of the brain involved in coordinating movements (the cerebellum), and other areas of the brain. This condition is also associated with the death of neurons in the spinal cord. Over time, the loss of cells

in the brain and spinal cord cells cause the signs and symptoms characteristic of SCA3.

Other Names for This Gene

- AT3
- ataxin-3
- ATX3
- ATX3_HUMAN

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of ATXN3 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=4287[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28ATXN3%5BTIAB%5D%29+OR+%28ataxin+3%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- ATAXIN 3; ATXN3 (https://omim.org/entry/607047)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/4287)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=ATXN3[gene])

References

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- Nicastro G, Masino L, Esposito V, Menon RP, De Simone A, Fraternali F, PastoreA. Josephin domain of ataxin-3 contains two distinct ubiquitin-binding sites.Biopolymers. 2009 Dec;91(12):1203-14. doi: 10.1002/bip.21210. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/19382171)

Genomic Location

The *ATXN3* gene is found on chromosome 14 (https://medlineplus.gov/genetics/chromosome/14/).

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