GAN Gene

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Gigaxonin

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1. Normal Function

The *GAN* gene provides instructions for making a protein called gigaxonin. Gigaxonin is part of the ubiquitin-proteasome system, which is a multi-step process that identifies and gets rid of excess or damaged proteins or structures (organelles) within cells. The ubiquitin-proteasome system tags unneeded proteins with a small protein called ubiquitin, marking them for destruction by a complex of enzymes called a proteasome. As part of this process, enzymes called E3 ubiquitin ligases recognize the specific proteins to be broken down and attach ubiquitin to them. Gigaxonin belongs to a group of E3 ubiquitin ligases called the Cul3-E3 ligases. It helps break down protein structures called intermediate filaments, which form networks that provide support and strength to cells.

In nerve cells (neurons), gigaxonin is thought to help break down specialized intermediate filaments called neurofilaments. Neurofilaments comprise the structural framework that establishes the size and shape of nerve cell extensions called axons, which are essential for transmission of nerve impulses.

2. Health Conditions Related to Genetic Changes

2.1 Giant Axonal Neuropathy

At least 47 mutations in the *GAN* gene have been identified in people with giant axonal neuropathy, an inherited disorder that causes gradually worsening loss of movement and sensation. Giant axonal neuropathy is characterized by abnormally large (giant) and deteriorating axons.

GAN gene mutations result in an unstable gigaxonin protein that breaks down easily, resulting in much less gigaxonin in cells than normal. In neurons, the reduction in gigaxonin leads to accumulation of neurofilaments that should have been destroyed by the ubiquitin-proteasome system. The neurofilaments become densely packed in the giant axons of people with giant axonal neuropathy. The giant axons are commonly seen in the peripheral nerves, which carry signals between the brain and spinal cord (central nervous system) and other areas of the body. However, axons in the central nervous system can be affected as well. These abnormal axons do not transmit signals properly and eventually deteriorate, causing severe problems in the peripheral nerves and the central nervous system.

3. Other Names for This Gene

- GAN1
- GAN_HUMAN
- giant axonal neuropathy (gigaxonin)
- KLHL16

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