FXN Gene

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Frataxin

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1. Normal Function

The *FXN* gene provides instructions for making a protein called frataxin. This protein is found in cells throughout the body, with the highest levels in the heart, spinal cord, liver, pancreas, and muscles used for voluntary movement (skeletal muscles). Within cells, frataxin is found in energy-producing structures called mitochondria. Although its function is not fully understood, frataxin appears to help assemble clusters of iron and sulfur molecules that are critical for the function of many proteins, including those needed for energy production.

One region of the *FXN* gene contains a segment of DNA known as a GAA trinucleotide repeat. This segment is made up of a series of three DNA building blocks (one guanine and two adenines) that appear multiple times in a row. In most people, the number of GAA repeats in the *FXN* gene is fewer than 12 (referred to as short normal). Sometimes, however, the GAA segment is repeated 12 to 33 times (referred to as long normal).

2. Health Conditions Related to Genetic Changes

2.1 Friedreich Ataxia

Friedreich ataxia results from an increased number of copies (expansion) of the GAA trinucleotide repeat in the *FXN* gene. In people with this condition, the GAA segment is abnormally repeated 66 to more than 1,000 times. The length of the GAA trinucleotide repeat appears to be related to the age at which the symptoms of Friedreich ataxia appear. People with GAA segments repeated fewer than 300 times tend to have a later appearance of symptoms (after age 25) than those with larger GAA trinucleotide repeats.

Most individuals with Friedreich ataxia have the expanded GAA trinucleotide repeat in both copies of the *FXN* gene. About 2 percent of people with this condition have an expanded GAA trinucleotide repeat in one copy of the *FXN* gene and a different kind of mutation in the other copy of the gene. In most of these cases, the other mutation changes a single DNA building block (nucleotide) within the *FXN* gene.

It is not fully understood how *FXN* gene mutations cause Friedreich ataxia. Mutations in this gene disrupt production of frataxin, greatly reducing the amount of this protein in cells. A shortage of frataxin appears to decrease the activity of proteins that contain iron-sulfur clusters, which could impair the production of energy in mitochondria. Cells with insufficient amounts of frataxin are also particularly sensitive to reactive molecules (free radicals) that can damage and destroy cells. Cells in the brain, spinal cord, and muscles that are damaged or have inadequate energy supplies may not function properly, leading to the signs and symptoms of Friedreich ataxia.

3. Other Names for This Gene

- CyaY
- FA
- FARR
- FRDA
- FRDA_HUMAN

- Friedreich ataxia
- MGC57199
- X25

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