TNNI3 Gene

Subjects: Genetics & Heredity
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Troponin I3, cardiac type: The TNNI3 gene provides instructions for making a protein called cardiac troponin I, which is found solely in the heart (cardiac) muscle.

genes

1. Normal Function

The *TNNI3* gene provides instructions for making a protein called cardiac troponin I, which is found solely in the heart (cardiac) muscle. Cardiac troponin I is one of three proteins that make up the troponin protein complex in cardiac muscle cells. The troponin complex is associated with a structure called the sarcomere, which is the basic unit of muscle contraction. Sarcomeres are made up of thick and thin filaments. The overlapping thick and thin filaments attach (bind) to each other and release, which allows the filaments to move relative to one another so that muscles can contract. The troponin complex, along with calcium, helps regulate tensing (contraction) of cardiac muscle.

For the heart to beat normally, cardiac muscle must contract and relax in a coordinated way. Cardiac troponin I helps to coordinate contraction of the heart. When calcium levels are low, the troponin complex binds to the thin filament. This binding blocks the interaction between the thick and thin filaments that is needed for muscle contraction. An increase in calcium levels causes structural changes in another troponin complex protein called troponin C, which then triggers the troponin complex to detach from the thin filament, allowing the heart muscle to contract.

2. Health Conditions Related to Genetic Changes

2.1. Familial hypertrophic cardiomyopathy

Mutations in the *TNNI3* gene can cause familial hypertrophic cardiomyopathy, a condition characterized by thickening (hypertrophy) of the cardiac muscle. *TNNI3* gene mutations are found in less than 5 percent of people with this condition. Although some people with hypertrophic cardiomyopathy have no obvious health effects, all affected individuals have an increased risk of heart failure and sudden death.

Most *TNNI3* gene mutations in familial hypertrophic cardiomyopathy change single protein building blocks (amino acids) in the cardiac troponin I protein. The altered protein is likely incorporated into the troponin complex, but it

may not function properly. It is unclear how these mutations lead to the features of familial hypertrophic cardiomyopathy.

In some people, hypertrophic cardiomyopathy develops into restrictive cardiomyopathy (described below), although it can be difficult to distinguish these two disorders.

2.2. Familial restrictive cardiomyopathy

Approximately 10 mutations in the *TNNI3* gene have been found to cause familial restrictive cardiomyopathy, which is characterized by stiffening of the heart muscle. Most of these mutations change single amino acids in the cardiac troponin I protein, which impairs the protein's function. The altered protein typically cannot bind to actin. As a result, heart muscle relaxation is disrupted, leading to abnormal heart function, impaired blood flow, and the signs and symptoms of familial restrictive cardiomyopathy, such as fatigue and fainting.

2.3. Other disorders

Mutations in the *TNNI3* gene can also cause another heart conditions called dilated cardiomyopathy. This condition weakens and enlarges the heart, preventing it from pumping blood efficiently. Dilated cardiomyopathy increases the risk of heart failure and premature death.

Familial dilated cardiomyopathy

3. Other Names for This Gene

- cardiac troponin I
- cTnI
- TNNI3_HUMAN
- troponin I type 3 (cardiac)
- troponin I, cardiac muscle

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