RYR2 gene

ryanodine receptor 2

Normal Function

The *RYR2* gene provides instructions for making a protein called ryanodine receptor 2. This protein is part of a family of ryanodine receptors, which form channels that transport positively charged calcium atoms (calcium ions) within cells.

Channels made with the ryanodine receptor 2 protein are found in heart (cardiac) muscle cells called myocytes. These channels are embedded in the outer membrane of a cell structure called the sarcoplasmic reticulum, which acts as a storage center for calcium ions. The RYR2 channel controls the flow of calcium ions out of the sarcoplasmic reticulum.

For the heart to beat normally, the cardiac muscle must tense (contract) and relax in a coordinated way. This cycle of muscle contraction and relaxation results from the precise control of calcium ions within myocytes. In response to certain signals, the RYR2 channel releases calcium ions from the sarcoplasmic reticulum into the surrounding cell fluid (the cytoplasm). The resulting increase in calcium ion concentration triggers the cardiac muscle to contract, which pumps blood out of the heart. Calcium ions are then transported back into the sarcoplasmic reticulum, and the cardiac muscle relaxes. In this way, the release and reuptake of calcium ions in myocytes produces a regular heart rhythm.

Health Conditions Related to Genetic Changes

Catecholaminergic polymorphic ventricular tachycardia

More than 200 mutations in the *RYR2* gene have been found to cause catecholaminergic polymorphic ventricular tachycardia (CPVT), a heart condition characterized by an abnormal heart rhythm (arrhythmia) during exercise or emotional stress, which can be fatal. Almost all of the *RYR2* gene mutations involved in CPVT change single protein building blocks (amino acids) in the ryanodine receptor 2 protein. These mutations alter the structure and function of the RYR2 channel.

Researchers are uncertain how *RYR2* gene mutations lead to ventricular tachycardia, the abnormally fast and irregular heart rhythm that is characteristic of CPVT. Some studies have suggested that mutations interfere with the regulation of the RYR2 channel.

Other studies have found that the altered RYR2 channel stays open abnormally, allowing calcium ions to "leak" out of the sarcoplasmic reticulum. It is clear that changes in the structure and function of the RYR2 channel disrupt the careful control of calcium ion flow in myocytes, which can trigger an abnormal heart rhythm in people with CPVT.

Arrhythmogenic right ventricular cardiomyopathy

Several other mutations in the *RYR2* gene have been found to cause a heart condition called arrhythmogenic right ventricular cardiomyopathy (ARVC). This condition causes part of the heart muscle to break down over time, which increases the risk of arrhythmia and sudden death.

The *RYR2* gene mutations responsible for ARVC change single amino acids in the ryanodine receptor 2 protein. These mutations alter the structure of the RYR2 channel, which probably allows calcium ions to "leak" out of the sarcoplasmic reticulum. This failure of calcium regulation within myocytes can trigger the abnormal heart rhythm characteristic of ARVC.

Familial atrial fibrillation

MedlinePlus Genetics provides information about Familial atrial fibrillation

Other Names for This Gene

- ARVC2
- ARVD2
- cardiac muscle ryanodine receptor
- cardiac muscle ryanodine receptor-calcium release channel
- CPVT1
- ryanodine receptor 2 (cardiac)
- VTSIP

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of RYR2 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=6262[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28RYR2%5BTIAB%5D%29+OR+%28ryanodine+receptor+2%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

- RYANODINE RECEPTOR 2; RYR2 (https://omim.org/entry/180902)
- VENTRICULAR TACHYCARDIA, CATECHOLAMINERGIC POLYMORPHIC, 1, WITH OR WITHOUT ATRIAL DYSFUNCTION AND/OR DILATED CARDIOMYOPATHY; CPVT1 (https://omim.org/entry/604772)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/6262)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=RYR2[gene])

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Genomic Location

The *RYR2* gene is found on chromosome 1 (https://medlineplus.gov/genetics/chromosome/1/).

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