We have over 20,000 different genes in the body. These genes are like instruction manuals for how to build a protein, and each protein has an important function that helps to keep our body working how it should. The *RYR1* gene makes a protein called a ryanodine receptor 1. This protein helps to move stored calcium from the sarcoplasmic reticulum (a structure in muscle cells that stores calcium) within the muscle cells. Calcium is involved in the contraction of the muscles; as calcium levels increase, the muscle contracts.

If there is a harmful error (called a pathogenic variant) in the *RYR1* gene, then it may not make as much of the ryanodine receptor 1 protein as the body needs. If there is not enough of the ryanodine receptor 1 protein, then calcium cannot be moved from the sarcoplasmic reticulum in the muscle cells as well. This can lead to increased levels of calcium in the muscle cells, which can prevent the muscle from contracting normally and can cause various different health problems.

Pathogenic variants in the *RYR1* gene account for approximately 70-80% of cases of malignant hyperthermia susceptibility (MHS), which can include a potentially life-threatening sensitivity to certain medications. Some specific pathogenic variants in the *RYR1* gene can cause other health issues, including congenital myopathies (muscle diseases that are there from birth, such as central core disease, congenital fiber-type disproportion, and multiminicore disease), and King-Denborough syndrome (which can cause myopathy, skeletal issues, MHS, and a characteristic facial appearance), among others. Because the *RYR1* gene is associated with MHS, it is generally suggested that all individuals with a *RYR1* pathogenic variant be treated as if they are at risk for MHS.

Pathogenic variants in the *RYR1* gene are most often inherited in an autosomal dominant pattern, meaning that anyone who carries the variant has a 50% chance to pass it down to any children they have. However, some pathogenic variants in *RYR1* can be passed down in a family in an autosomal recessive pattern, which means that someone must inherit a nonworking gene from BOTH parents in order to develop the medical condition. Women and men both have the *RYR1* gene and have the same chances to inherit and pass down pathogenic variants. Due to the complexity of the pathogenic variants in the *RYR1* gene, it is important to talk with a specialist, such as a geneticist or genetic counselor, to learn more about how they can affect you and your family.

Genetic Testing for *RYR1*

Genetic testing for pathogenic variants in *RYR1* is currently available, but there are a few different ways to approach testing:

- *Single site analysis*: Testing specific to a known pathogenic variant in the family
- Full gene sequencing and rearrangement analysis: Comprehensive testing to search for all currently detectable pathogenic variants in the gene
- Gene panels: Newer, more broadly based gene tests that would include not only the *RYR1* gene, but other genes known or suspected to be associated with health concerns like those that can be related to *RYR1*.

Click here to learn more about scheduling a genetic counseling appointment for questions about pediatric or adult genetic conditions.