

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 *LMNA* gene makes proteins called lamins. Our body is made up of billions of cells, and there are many parts of the cell. The 'mothership' of the cell is called the nucleus. The nucleus holds our DNA and helps to protect and regulate it. The nuclear envelope surrounds the nucleus to help protect it, and to monitor different things that travel in and out of the nucleus. Lamins work to support the nuclear envelope and make sure that the nucleus is protected. Some studies have also suggested that lamins may play a part in how our genes are expressed.

If someone has a harmful change (called a pathogenic variant) in one of their *LMNA* genes, then their body does not make as much lamin protein as it should. If there is not enough lamin protein, then the nucleus is not as well protected. This leads to a higher rate of cell death and damage because the nucleus of the cells are more vulnerable. This progressive cell death is what can damage the heart muscles, which can lead to several different types of health issues, including arrhythmogenic right ventricular cardiomyopathy, familial dilated cardiomyopathy, and left ventricular noncompaction.

Pathogenic variants in the *LMNA* gene are passed through the family in an <u>autosomal</u> <u>dominant</u> pattern, meaning that anyone who carries a pathogenic variant has a 50% chance to pass it down to any children they have. Women and men both have the *LMNA* gene and have the same chances to inherit and pass down pathogenic variants.

Genetic Testing for LMNA

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

- <u>Single site analysis</u>: Testing specific to a known pathogenic variant in the family
- Full gene <u>sequencing</u> and <u>rearrangement analysis</u>: Comprehensive testing to search for all currently detectable pathogenic variants in the gene
- <u>Gene panels</u>: Newer, more broadly based gene tests that would include not only the *LMNA* gene, but other genes known or suspected to be associated with hereditary heart disease.

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