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 *LDLR* gene makes a protein called a low-density lipoprotein receptor (LDL-r). This LDL-r attaches to LDL cholesterol that is floating around in our blood and brings it into our cells. Our cells can then either use, store, or get rid of the cholesterol.

The LDL-r protein is most active in the liver, which is the organ that removes most of the extra cholesterol in our bodies. The amount of the LDL-r protein in the liver determines how fast the liver can remove extra cholesterol from the bloodstream. If there is a harmful error (called a pathogenic variant) in the *LDLR* gene, then it may not make as much of the LDL-r protein as the body needs. If there is not enough of the LDL-r protein, then the liver can not clear extra cholesterol from the bloodstream as quickly. This can lead to the cholesterol building up in the body, which can cause the signs and symptoms we associate with familial hypercholesterolemia.

Recent studies have shown that only approximately 73% of people who carry a pathogenic variant in the *LDLR* gene have significantly elevated LDL cholesterol level. This means that some individuals in the family may carry this variant, and could potentially pass it down to their children, but have no obvious signs or symptoms.

Pathogenic variants in the *LDLR* gene are passed through a family 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. Women and men both have the *LDLR* gene and have the same chances to inherit and pass down pathogenic variants. Almost all people who have a pathogenic variant in the *LDLR* gene have a parent who also carries it.

Genetic Testing for *LDLR*

Genetic testing for pathogenic variants in *LDLR* 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 *LDLR* gene, but other genes known or suspected to be associated with familial hypercholesterolemia

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