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 *APOB* gene makes a protein called apolipoprotein B. Apolipoprotein B proteins perform many jobs in the body, including helping to carry fat and cholesterol from our intestines into our bloodstream. It also helps to attach cholesterol to LDL receptors (made by the *LDLR* gene) on our cells, which bring cholesterol into the cells where it can be used, stored, or gotten rid of. This process or removing excess cholesterol happens primarily in the liver.

The amount of the apolipoprotein B protein that is in the body determines how well the cholesterol can attach to the the LDL receptors. If someone has a harmful error (called a pathogenic variant) in one of their *APOB* genes, then their body is not going to make enough of the apolipoprotein B protein as it should. If there is not enough apolipoprotein B, then the cholesterol cannot be captured and processed as easily by the cells. This can lead to the cholesterol building up in the body, which can cause the signs and symptoms we associated with familial hypercholesterolemia.

Recent studies have shown that people who have FH that is caused by a pathogenic variant in the *APOB* gene tend to be less severe than those who carry pathogenic variants in the *LDLR* or *PCSK9* genes.

Pathogenic variants in the *APOB* 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 *APOB* gene and have the same chances to inherit and pass down pathogenic variants. Almost all people who have a pathogenic variant in the *APOB* gene have a parent who also carries it.

Genetic Testing for *APOB*

Genetic testing for pathogenic variants in *APOB* 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 *APOB* 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.