

Genetic Testing Familial Hypercholesterolemia (FH)

Possible Indications for Use:

- Family history of familial hypercholesterolemia¹
- Known familial mutation in *LDLR*, *ApoB*, or *PCSK9* genes¹
- Diagnosis of FH not certain²

Benefits:

- May confirm a clinical diagnosis of FH in the index patient and family members¹
- May allow early diagnosis in family members, enabling early intervention, which may prevent or repair atherosclerotic damage and lower the risk of coronary heart disease²
- In some cases, may predict the severity of disease based on the exact mutation (and zygosity) found¹
- May instill motivation to implement appropriate treatment regimens²

Background:

- FH is a common, heritable metabolic disease characterized by severely elevated cholesterol levels, which, if untreated, may significantly increase the risk of early-onset coronary heart disease.
- Affecting about 1 in 300-500, FH is inherited in an autosomal dominant fashion and, in rare cases (1 in 1 million), may exhibit codominant inheritance wherein homozygotes are much more severely affected than heterozygotes.^{2,3}
- About 85% to 95% of FH cases are caused by mutations of the *LDLR* gene.² An *APOB* mutation accounts for 5% to 10% of cases, and *PCSK9* mutations cause less than 5% of cases.² Early detection of FH is important, since early detection and long-term treatment of FH can significantly reduce the risk of coronary heart disease.²
- FH is usually diagnosed by traditional lipid testing, an assessment of family history, and, in severe cases, the presence of clinical signs such as tendon xanthomata or cornea arcae in the proband.¹ However, the absence of these clinical signs does not exclude a diagnosis of FH.²
- Since published studies have established a clear causal relationship between sequence variants in the *LDLR*, *ApoB*, and *PCSK9* genes and FH, diagnosis of FH may also be achieved through genetic testing.¹⁻³ However, a negative genetic test does not exclude a diagnosis of FH.

References: 1. Izar MC, et al (2010) *The Application of Clinical Genetics* 3:147-157.
2. Goldberg AC, et al (2011) *J Clin Lipidol* 5:133-140. 3. Varret M, et al (2008) *Clin Genet* 73:1-13.

Ordering Information: Please see other side.



Ordering Information for the *LDLR*, *APOB* and *PCSK9* DNA Sequencing Tests (Familial Hypercholesterolemia- FH)

Indications for Testing

- Family history of familial hypercholesterolemia
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Ordering Information

Gene(s)	Test Code
<i>LDLR</i>	190101
<i>APOB</i>	190102
<i>PCSK9</i>	252873

Multi-Gene Panel*

<i>LDLR, APOB</i>	190199
<i>LDLR, APOB, PCSK9</i>	252880

* For the multi-gene panel, a summary report will be issued in addition to an abbreviated report for each individual gene.

Family Testing (single amplicon)

Family Testing is available for both genes. Please contact Client Services at 1-866-647-0735 for requirements.

Test Methodology

- Amplification by polymerase chain reaction (PCR); sequencing of protein-coding region

NOTE: Specimens must be accompanied by a completed consent form. In the case of family tests (ie, known mutations), a copy of the result of the first patient tested in the family (the index case) must be submitted unless that test was performed at Correlagen. Other family members are subsequently tested for the specific mutation found in the first patient tested.

For test information, sample requirements, or to request a sample shipping kit, please contact Client Services at 1-866-647-0735 or visit us on the web at www.correlagen.com.