Cincinnati Children's
Heart Institute

Heart Institute Diagnostic Lab
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Familial Hypercholesterolemia

LDLR Full Gene Sequencing
APOB (R3500W and R3500Q) Sequencing

Familial Hypercholesterolemia (FH) is characterized by elevated LDL cholesterol levels which can lead to atherosclerotic plaque depositions in the arteries. FH is associated with a markedly increased risk of coronary artery disease at a young age. Deposits of cholesterol can also be seen in tendons (xanthomas) or around the eyes (xanthelasmas). Individuals with FH commonly have coronary heart disease, which can be associated with angina, myocardial infraction, and stroke.

The prevalence of heterozygous FH is estimated to be 1:200-500. Untreated individuals have a 20-fold increased risk for coronary heart disease. The diagnosis of FH can be confirmed by the presence of a pathogenic variant in genes associated with FH. Mutations, including deletions and duplications, in *LDLR* can be identified in 60-80% of individuals with FH. Pathogenic variants in *APOB* account for about 1-5% of FH cases, with R3500W and R3500Q mutations being the most common. FH is an autosomal dominant condition; however, homozygous FH can occur with a more severe phenotype.

Indication

Genetic testing for FH is indicated for individuals with clinical suspicion for FH.

Currently available tests include:
LDLR Full Gene Sequencing
LDLR Known Mutation Sequencing
APOB (R3500W/R3500Q) Analysis

Shipping Instructions

Please enclose a test requisition form with sample. All information must be complete before sample can be processed. Samples may be shipped at room temperature by overnight Federal Express to arrive Monday through Friday.

Ship To:

Cincinnati Children's
Hospital Medical Center
Attn: Heart Institute Diagnostic Lab
240 Albert Sabin Way,
Room S4.381
Cincinnati, OH 45229-3039

Methodology:

All 18 coding exons, as well as the exon/intron boundaries and portion of untranslated regions of the *LDLR* gene (NM_000527.4) are amplified by PCR for *LDLR* full gene sequencing analysis. A region harboring the R3500 of the *APOB* gene is amplified by PCR for the *APOB* (R3500W and R3500Q) sequencing test. Genomic DNA sequences from both forward and reverse directions are obtained by automatic fluorescent detection using an *ABI PRISM® 3730 DNA Analyzer*. Sequence variants different from National Center for Biotechnology Information GeneBank reference are further evaluated for genetic significance. If a mutation is identified, a known familial mutation analysis will be available for additional family members.

Sensitivity & Accuracy:

Greater than 99% of the sequencing mutations in exons 1-18 of *LDLR* and *APOB* R3500W and R3500Q mutations are detectable by this method. Sequencing does not detect large DNA rearrangements, deletions/duplications or low level mosaicism.

References:

Goldberg AC, et al. Familial hypercholesterolemia: Screening, diagnosis and management of pediatric and adult patients: Clinical guidance from the national lipid association expert panel on familial hypercholesterolemia. *Journal of Clinical Lipidology*. 2011;5:S1-8.

Identification and management of familial hypercholesterolaemia (FH). London; 2008.

Youngblom E, Knowles JW. Familial hypercholesterolemia. In: Pagon RA, Adam MP, Ardinger HH, Wallace SE, Amemiya A, Bean LJH, Bird TD, Dolan CR, Fong CT, Smith RJH, Stephens K, eds. *Genereviews(r)*. Seattle (WA); 1993.

Specimen:

Peripheral blood in EDTA tube
Adult: 3-5mL
Child: 3-5mL
Infant: 1-3mL
For other specimen types, please contact Amy Shikany at 513-803-3317

Turnaround Time:

LDLR Full Gene Analysis 2-4 weeks
LDLR Known Mutation Analysis 1-2 weeks
APOB (R3500W/R3500Q) Analysis 1-2 weeks

CPT Codes:

LDLR Full Gene Sequencing: 81406
LDLR Known Sequencing: 81403
APOB (R3500W/R3500Q) Analysis: 81479