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
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:


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


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