

Hypercholesterolemia Panel: Sequencing and CNV Analysis

Test Code: MM540

Turnaround time: 6 weeks

CPT Codes: 81479 x1, 81401 x1, 81406 x1

Condition Description

Hereditary hypercholesterolemia may cause the buildup of excess cholesterol in tissues. If cholesterol accumulates in tendons, it causes characteristic growths called tendon xanthomas. Yellowish cholesterol deposits under the skin of the eyelids are known as xanthelasmata. Cholesterol may also accumulate at the edges of the cornea, leading to a grey-colored ring called an arcus cornealis.

The most common inherited form of high cholesterol is called familial hypercholesterolemia, which can be inherited in an autosomal dominant or autosomal recessive pattern. This condition affects about 1 in 500 people in most countries. Familial hypercholesterolemia occurs more frequently in certain populations, including Afrikaners in South Africa, French Canadians, Lebanese, and Finns.

Most cases of high cholesterol are not caused by a single inherited condition, but result from a combination of lifestyle choices and the effects of variations in many genes.

Reference:

- GeneReviews

Genes

[ABCA1](#), [ABCG5](#), [ABCG8](#), [ANGPTL3](#), [APOA1](#), [APOA5](#), [APOB](#), [APOC2](#), [APOC3](#), [APOE](#), [CETP](#), [GPD1](#), [GPIHBP1](#), [LCAT](#), [LDLR](#), [LDLRAP1](#), [LIPA](#), [LIPC](#), [LME1](#), [LPL](#), [MTTP](#), [PCSK9](#), [SAR1B](#), [SCARB1](#)

Indications

The test is indicated for:

- Individuals with a clinical or suspected diagnosis of an hypercholesterolemia.

Methodology

Next Generation Sequencing: In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

Copy Number Analysis: Comparative analysis of the NGS read depth (coverage) of the targeted regions of genes on this panel was performed to detect copy number variants (CNV). The accuracy of the detected variants is highly dependent on the size of the event, the sequence context and the coverage obtained for the targeted region. Due to these variables and limitations a minimum validated CNV size cannot be determined; however, single exon deletions and duplications are expected to be below the detection limit of this analysis.

Detection

Next Generation Sequencing: Clinical Sensitivity: Unknown. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical/biochemical phenotype.

Analytical sensitivity for sequence variant detection is ~99%.

Copy Number Analysis: The sensitivity and specificity of this method for CNV detection is highly dependent on the size of the event, sequence context and depth of coverage for the region involved. The assay is highly sensitive for CNVs of 500 base pairs or larger and those containing at least 3 exons. Smaller (< 500 base pairs) CNVs and those that involving only 1 or 2 exons may or may not be detected depending on the sequence context, size of exon(s) involved and depth of coverage.

Specimen Requirements

Type: DNA, Isolated

Specimen Requirements:

Microtainer

8µg

Isolation using the Perkin Elmer™ Chemagen™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping:

Refrigerate until time of shipment in 100 ng/μL in TE buffer. Ship sample at room temperature with overnight delivery.

Type: Saliva**Specimen Requirements:**

Oragene™ Saliva Collection Kit

Orangene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

Specimen Collection and Shipping:

Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

Type: Whole Blood (EDTA)**Specimen Requirements:**

EDTA (Purple Top)

Infants and Young Children (2 years of age to 10 years old): 3-5 ml

Older Children & Adults: 5-10 ml

Autopsy: 2-3 ml unclotted cord or cardiac blood

Specimen Collection and Shipping:

Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.