Hypercholesterolemia: Sequencing Panel

Test Code: MM540
Turnaround time: 6 weeks
CPT Codes: 81401 x1, 81406 x1, 81479 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, GPIHB1, LCAT, LDLR, LDLRAP1, LIPA, LIPC, LMF1, LPL, MMTP, 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.

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. Large deletions/duplications will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical/biochemical phenotype.

Analytical Sensitivity: ~99%.

Specimen Requirements

Submit only 1 of the following specimen types

Type: Whole Blood

Specimen Requirements:

In EDTA (purple top) tube:
Infants (2 years): 3-5 ml
Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Ship sample at room temperature with overnight delivery.

Type: Isolated DNA

Specimen Requirements:
In microtainer: 60 ug

Isolation using the Qiagen\textsuperscript{TM} Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping: Refrigerate until time of shipment in 100 ng/ul of TE buffer. Ship sample at room temperature with overnight delivery.