FAMILIAL
HYPERCHOLESTEROLEMIA
FOCUSED PANEL

London Health Sciences Centre
St JOSEPH's HEALTH CARE LONDON
Pathology and Laboratory Medicine

Orderable – E-order/Requisition

Turnaround Time: 4-6 weeks

Laboratory:
Molecular Diagnostics Lab

Requisition:
Familial Hypercholesterolemia Ontario Requisition

Test Schedule:
As required,
Monday to Friday 0800-1600 hours

Alternate Name(s):

Dyslipidemia Focused Panel

Panel Content:

8 Genes; ABCG5, ABCG8, APOB, APOE, LDLR, LDLRAP1, LIPA, PCSK9

Specimen:

2 x 4mL whole blood in Lavender EDTA top Vacutainer tube

Collection Information:

Sample may be transported at room temperature

Method of Analysis:

All coding exons and 20 bp of flanking intronic sequence are enriched using a LHSC custom targeted hybridization protocol (Roche), followed by high throughput sequencing (Illumina). Sequence variants and copy number changes are assessed and interpreted using clinically validated algorithms and commercial software (SoftGenetics: Nextgene, Geneticist Assistant, Mutation Surveyor; and Alamut Visual). All exons have >200x mean read depth coverage, with a minimum 50x coverage at a single nucleotide resolution. Variants interpreted as either ACMG category 1, 2, or 3 (pathogenic, likely pathogenic, VUS; PMID: 25741868) are confirmed using Sanger sequencing, MLPA, or other assays when necessary. ACMG category 4 and 5 variants (likely benign, benign) are not reported, but are available upon request. This assay has been validated at a level of sensitivity equivalent to the Sanger sequencing and standard copy number analysis (>99%; PMID: 27376475, 28818680). Sample fidelity is assessed by matching sequencing results with the Exome QC genotyping assay (Agena).

Reference Ranges:

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See report

Interpretive Comments:

Abnormal lipid levels (dyslipidemias) are the major drivers of atherosclerosis, one of the major risk factors for cardiovascular disease (CVD). Familial hypercholesterolemia (FH) is one of the most common monogenic disorders, affecting approximately 1 in 250-300 Canadians, yet is underdiagnosed in Canada and worldwide. DNA-based test is a component of the diagnostic algorithms for dyslipidemias as described by the Simon Broome Register criteria (Marks et al., 2003) the Dutch Lipid Clinic Network criteria (Fouchier et al., 2001) and the Canadian Cardiovascular Society (Ruel et al., 2018). This Familial Hypercholesterolemia/Dyslipidemia panel test is a deep sequencing NGS assay designed based on guidance from the Ontario Health-FH Working Group and clinical specialists.

Storage and Shipment:

Sample must be received in testing laboratory within 4 days of collection; shipped at room temperature by courier/overnight delivery