CHARCOT MARIE TOOTH DISEASE

London Health Sciences Centre | St. Joseph's Health Care London

Pathology and Laboratory Medicine

Orderable – E-order/Requisition

Turnaround Time: 4-6 weeks **STAT: 4 weeks**

Alternate Name(s):

CMT
Charcot Marie Tooth Neuropathy

Laboratory:
Molecular Diagnostics Lab

Specimen:

Whole blood-2 x 4 mL Lavender EDTA top Vacutainer tube

Requisition:
MOLECULAR DIAGNOSTIC REQUISITION

Collection Information:

Blood samples must be maintained at room temperature.

Method of Analysis:
All coding exons and 20 bp of flanking intronic sequence are enriched using an LHSC custom targeted hybridization protocol (Roche Nimblegen), 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 >300x mean read depth coverage, with a minimum 100x coverage at a single nucleotide resolution. This assay meets the sensitivity and specificity of combined Sanger sequencing and

Reference Ranges:

See report

Interpretive Comments:

Charcot-Marie-Tooth (CMT) disease is a genetically and clinically heterogeneous group of inherited disorders of the peripheral nervous system characterized by progressive loss of muscle tissue and touch sensation across various parts of the body. CMT type 1 (CMT1) is a demyelinating peripheral neuropathy characterized by distal muscle weakness and atrophy, sensory loss, and slow nerve conduction velocity. CMT type 2 (CMT2) is an axonal (non-demyelinating) peripheral neuropathy characterized by distal muscle weakness and atrophy, mild sensory loss, and normal or near-normal nerve conduction velocities. Most common mutation is associated with CMT1A (70%-80% of all CMT1) and involves duplication of PMP22, while PMP22 gene deletion is the most common cause (80%) of hereditary neuropathy with liability to pressure palsies (HNPP). Mutations in remaining genes are associated with less frequent subtypes of CMT, including autosomal dominant, recessive and X-linked forms of the disease.

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Specimen Stability:

Must be received in testing laboratory within 5 days of collection, shipped at room temperature by courier/overnight delivery.

MLPA copy number analysis. All 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. 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).

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