EGL Genetics | Eurofins Clinical Diagnostics

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Hereditary Neuropathies Panel: Sequencing and CNV Analysis

Test Code: MM350
Turnaround time: 6 weeks
CPT Codes: 81325 x1, 81403 x1, 81404 x1, 81405 x1, 81406 x1, 81407 x1, 81408 x1, 81260 x1

Condition Description

Hereditary neuropathies are a collection of inherited disorders affecting the peripheral nervous system. The hereditary neuropathies are divided into four major subcategories: hereditary motor and sensory neuropathy, hereditary sensory neuropathy, hereditary sensory and autonomic neuropathy, and hereditary motor neuropathy. Charcot-Marie-Tooth disease, is of the most common types of the hereditary motor and sensory neuropathies. Clinical presentation typically includes sensory symptoms like pain in the feet and hands, motor symptoms such as weakness in the lower leg and feet muscles. Some hereditary neuropathies can affect the autonomic nerves, resulting in impaired sweating, postural hypotension, or insensitivity to pain.

The estimated prevalence of hereditary neuropathies is about 1 in 2500 individuals. A myriad of genes are associated with hereditary neuropathies. Genetic testing has therefore become an important tool in the diagnosis of neuropathies.

References:

- Sagnelli et al. (2013) *J Neurol.* 260(10):2684-90.
- Auer-Grumbach M. (2013) *Handb Clin Neurol.* 115:893-906.
- Murphy et al. (2013) *Handb Clin Neurol.* 2013;115:213-32.

Genes

AARS1, ALDH3A2, APTX, ATL1, ATM, ATP7A, BSCL2, CACNB4, COQ8A, CTDP1, DCTN1, DNAJB2, DNM2, DNMT1, DYNC1H1, EGR2, ELP1, FGD4, FGF14, FIG4, FXN, GAN, GARS1, GDAP1, GJB1, GLA, HOXD10, HSPB1, HSPB8, IGHMBP2, ITPR1, KCNA1, KCNC3, KIF1A, KIF1B, KIF5A, L1CAM, LITAF, LMNA, LRSAM1, MED25, MFN2, MPZ, MRE11, MTMR2, MTTP, NDRG1, NEFL, NGF, NIPA1, NTRK1, PEX7, PHYH, PLEKHG5, PLP1, PMP22, PNPLA6, POLG, PRKCG, PRPS1, PRX, RAB7A, REEP1, RETREG1, SACS, SBF2, SCN9A, SH3TC2, SIL1, SLC12A6, SLC1A3, SPART, SPAST, SPG11, SPG21, SPG7, SPTBN2, SPTLC1, SPTLC2, TDP1, TRPV4, TTBK2, TTPA, TTR, TWNK, WASHC5, WNK1, YARS1, ZFYVE26, ZFYVE27

Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of a neuropathy.

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. Pathogenic variants in the promoter region, some pathogenic variants in the introns and other regulatory element pathogenic variants cannot be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical and/or 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

Submit only 1 of the following specimen types

Type: Whole Blood (EDTA)

Specimen Requirements:

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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.

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: 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.

Related Tests

- Charcot-Marie-Tooth (*PRPS1* Gene Sequencing and Deletion/Duplication Analysis)
- Hereditary Neuropathies: Deletion/Duplication Panel

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