Neuromuscular Disorders: Sequencing Panel

Test Code: MNEU1
Turnaround time: 6 weeks
CPT Codes: 81404 x1, 81405 x1, 81406 x1, 81407 x1, 81408 x1, 81400 x1, 81401 x1

Condition Description

The neuromuscular disorders (NMD) are a group of conditions that affect the peripheral nervous system and muscles. Primarily, they affect the ability to perform voluntary movements. They range in onset from before a child is born to much later in life with the majority beginning during infancy, childhood, or the teenage years. With many of the neuromuscular disorders overlapping in their clinical and/or pathological phenotypes, molecular testing can be necessary to pinpoint the precise disorder a patient has.

The Neuromuscular Disorders Panel includes testing for nemaline myopathy, limb girdle muscular dystrophy, Emery-Dreifuss muscular dystrophy, congenital muscular dystrophy, Zellweger syndrome spectrum, and cardiomyopathies. Individual disorders included on this panel are myoadenylate deaminase deficiency, erythrocyte AMP deaminase deficiency, myofibrillar myopathy, Duchenne/Becker muscular dystrophy, congenital disorder of glycosylation type 1a, malignant hyperthermia susceptibility, myoclonus dystonia, Marinesco-Sjogren syndrome, and distal arthrogryposis.

Note: This test does not detect the retrotransposon insertion in the 3' UTR of the \( FKTN \) gene common in some Asian populations. For patients with suspected Fukuyama congenital muscular dystrophy, testing for the \( FKTN \) insertion is recommended. Analysis for the \( FKTN \) insertion is available as a separate assay.

Reference:

Genes

\( ACTA1, AMPD1, ANOS, CAPN3, CAV3, COL6A1, COL6A2, COL6A3, CRPPA, DES, DMD, DYSF, EMD, FKRP, FKTN, GAA, GNE, ITGA7, LAMA2, LARGE1, LMNA, MYOT, NEB, PLEC, PMM2, POMGNT1, POMT1, POMT2, PYGM, RYR1, RYR2, SELENON, SGCA, SGCB, SGCD, SGCE, SGCG, SIL1, TCAP, TNNI2, TNNT1, TPM2, TPM3, TRIM32, TTN, VCP \)

Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of neuromuscular disorders.

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: 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™ 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: 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 24 hours of collection. Do not refrigerate or freeze.

Related Tests

- Single-gene testing is available for most genes on this panel.
- Limb-Girdle Muscular Dystrophy: Sequencing Panel.
- Congenital Muscular Dystrophy: Sequencing Panel.
- Bethlem Myopathy/Ullrich Congenital Muscular Dystrophy Panel.
- Expanded Neuromuscular: Sequencing Panel.
- Neuromuscular Disorders: Deletion/Duplication Panel.