 Expanded Neuromuscular Disorders: Sequencing Panel

**Condition Description**

Neuromuscular disorders (NMDs) collectively refer to the many disorders that affect the peripheral nervous system either by impairing the proper development or functioning of muscles, or by damaging the associated nerves or neuromuscular junctions. NMDs comprise over 200 Mendelian disorders, all of which are rare individually, but have an approximate disease prevalence of 1 in 3,000 altogether. Of the inherited NMDs, muscular dystrophies are the most common. Muscular dystrophies are highly heterogeneous muscle disorders that share clinical, genetic, and pathological characteristics; their major clinical characteristics include muscle degeneration and wasting, progressive muscle weakness, hypotonia, and elevated serum creatine kinase levels.

The expanded neuromuscular panel includes a wide range of clinical presentation and heterogeneity. They include muscular dystrophies, congenital myopathies, and congenital myasthenic syndrome. Over the past few years a number of genes with overlapping clinical phenotypes have been identified in neuromuscular disorders.

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.

**References:**


**Genes**

ACTA1, AMPD1, ANOS1, BAG3, BIN1, BSCL2, CAPN3, CAV3, CAVIN1, CFL2, CHAT, CHRNA1, CHRNB1, CHRND, CHRNE, CHRNQ, COL6A1, COL6A2, COL6A3, COLQ, CRYAB, DAG1, DES, DMD, DNM2, DOK7, DYSF, EMD, FHL1, FKRP, FKN, FLNC, GAA, GLE1, GNE, IGHMBP2, ISP2, ITGA7, LAMA2, LARGE1, LDB3, LMNA, MTM1, MTM14, MUSK, MYH2, MYH7, MYOT, NEB, PABPN1, PLEC, PLEKHG5, PMM2, POMGNT1, POM1, POMT1, POMT2, PYGM, RAPSN, RYR1, RYR2, SCN4A, SELENON, SGCA, SGCB, SGCD, SGCE, SGCG, SIL1, SYNE1, TCAP, TNNT1, TPM2, TPM3, TRIM24, TTN, VCP, VRK1

**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: 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™ 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.

**Related Tests**

- Neuromuscular Disorders Panel.
- Limb-girdle Muscular Dystrophy Panel.
- Congenital Muscular Dystrophy Panel.
- Expanded Neuromuscular Disorders: Deletion/Duplication Panel.