Dystonia Panel: Sequencing and CNV Analysis

**Test Code:** MM550  
**Turnaround time:** 6 weeks  
**CPT Codes:** 81321 x1, 81404 x5, 81405 x8, 81406 x11, 81407 x1, 81408 x1, 81290 x1, 81184 x1, 81479 x1

**Condition Description**

Dystonia is a movement disorder affecting 1-2 people per 10,000 and is characterized by prolonged or intermittent muscle contractions resulting in abnormal movement or body postures that can be painful. Some forms may involve involuntary actions such as closing of the eyelids or larynx. Dystonia can affect one part of the body or can be generalized across multiple muscle groups. In addition, complex dystonia syndromes have the prolonged muscle contraction as a major manifestation, but other neurological signs or atypical features are also present. There are non-genetic causes such as infection, medications, and vascular or hypoxic insults to the body, but most forms of dystonia have genetic causes. Although most dystonia and dystonic syndromes are inherited in an autosomal dominant manner, autosomal recessive and x-linked forms also exist. All of these factors make diagnosing the exact type/cause of dystonia extremely difficult.

Testing one suspected gene at a time can be both costly and time-consuming. Gene panels offer healthcare providers the ability to cast a wider net when searching for a diagnosis. Certain diagnoses can provide better guidance for prognosis, treatment, and recurrence.

**References:**


**Genes**

ADAR, AFG3L2, ANO3, AP1S2, APTX, ARSA, ARX, ATM, ATP13A2, ATP1A2, ATP1A3, ATP7B, AUH, C19orf12, CACNA1A, CHMP2B, COL6A3, CP, CYP27A1, DCAF17, DDC, DLAT, DRD2, DRD5, EARS2, ERCC6, F2H, FASTKD2, FBXO7, FOXG1, FOXRED1, GATM, GCDD, GCH1, GNAL, HPCA, HPRT1, KCNQ2, KMT2B, L2HGDH, MAT1A, MCOLN1, MMADHC, MPV17, NPC2, PANK2, PDPFRB, PDX1, PINK1, PLATG, PLP1, PINKD, PNPT1, PRKN, PRTT2, PSEN1, PSEN2, PTEN, PTS, QDPR, RNASEH2A, RNASEH2B, RNASEH2C, SAMHD1, SCP2, SDHAF1, SERAC1, SGCCE, SLC19A3, SLC20A2, SLC2A1, SLC30A10, SLC4A1, SLC6A3, SPR, SULCL2, SUOX, TAF1, TH, THAP1, TIMM8A, TOR1A, TP51, TREM2, TREX1, VPS37A, WDR45

**Indications**

The test is indicated for:

- Individuals with a clinical or suspected diagnosis of dystonia.

**Methodology**

**Next Generation Sequencing:** In solution hybridization of all coding exons contained in the genes of the Dystonia Panel is performed on the patient’s genomic DNA. Direct sequencing of the amplified 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 in order to confirm variants and ensure 100% coverage of the targeted exons. Sequence variations are classified as pathogenic variants, benign variants unrelated to disease, or variants of unknown clinical significance. Variants of unknown clinical significance may require further studies of the patient and/or family members. This assay does not interrogate the promoter region, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications.

**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. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical/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: Saliva

Specimen Requirements:
Oragene™ Saliva Collection Kit
Oragene™ 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: 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 72 hours of collection. Do not freeze.

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.