Mitochondrial-Membrane Protein-Associated Neurodegeneration (MPAN), *C19orf12*, Sequencing

**Test Code:** 1145  
**Department:** Molecular Genetics

**Test Synonyms:**  
C19orf12

**CPT Code(s):**  
83891  
83898 x 3  
83892 x 3  
83904 x 3  
83909 x 3

**Background:**  
Mitochondrial-membrane Protein-Associated Neurodegeneration (MPAN) is characterized by progressive dystonia, spasticity, paraparesis or tetraparesis, optic atrophy, psychiatric changes (ADHD-like behavior, mood swings), and evidence of iron accumulation in both the globus pallidus and substantia nigra on T2-weighted MRI. Onset generally occurs in childhood to early adulthood with slow progression and survival well into adulthood. MPAN is observed in ~10% of NBIA patients and mutations in *c19orf12* are observed in 95% of patients with a clinical diagnosis of MPAN. Mutations in MMIN are observed in ~40% of patients with a negative mutation test for other NBIA-associated genes, eg. PANK2, PLA2G6, CP and FTL (Hartig et al. 2011).

**Reasons for Referral:**  
- Confirmation of a suspected diagnosis in patients with the hallmark findings of MPAN  
- Further assessment of patients with clinical diagnosis of idiopathic Neurodegeneration with Brain Iron Accumulation (NBIA) who do not have an eye-of-the-tiger sign and/or have had mutations ruled out in PANK2 or PLA2G6.  
- Carrier testing of family members of MPAN patients with known mutations.

**Methodology:**  
Testing for *c19orf12* mutations in MPAN is performed by sequence analysis of all three exons of the *c19orf12* gene. All exons and exon/intron junctions are amplified by PCR and are sequenced in both directions. Full gene sequencing is anticipated to have a yield greater than 95%. All nucleotide changes are analyzed in the context of current databases and literature, and using web-based prediction algorithms, in order to determine or predict pathogenicity.

**Specimen Requirements:**  
- Blood: EDTA or ACD (Solution A or B):  
  - Adult: 5mL  
  - Child: 5mL  
  - Infant: 2-3mL  

_A REQUISITION FORM MUST ACCOMPANY ALL SAMPLES._ Please include detailed clinical information, including ethnicity, clinical history, and family history.

**Test Performed (Days):**  
Weekly
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**Turn Around Time:**
14 – 21 days

**Shipment Sensitivity Requirements:**
Keep specimen cold during transit, but do not ship on dry ice. Please contact Client Services at (855) 535-1522 for shipping kits and instructions. Use the cold pack provided in the KDL shipping kit. Ship the specimen overnight express, using the FedEx priority overnight label provided. The specimen must arrive at the lab no more than 24 hours after collection.

**References:**