MEDICAL DIAGNOSTIC LABORATORIES, L.L.C.

INTERPRETATION GUIDELINES

Torsion Dystonia by Real-Time PCR

Methodology: This Torsion Dystonia test screens for two mutations in the TOR1A gene: delGAG and del18bp. This assay is performed in a Real-Time PCR format utilizing two separate PCR reactions targeting the GAG and 18bp deletions.

Result	Comment	Interpretation
Not Detected	Mutations: No mutations detected	This individual tested negative for the four mutations listed.
Positive	Mutation Detected: delGAG (HT)	delGAG heterozygote (HT) - One copy of the delGAG mutation was identified indicating that this individual is a carrier for Torsion dystonia. This interpretation is based on the assumption that this individual is not clinically affected with Torsion dystonia. Genetic counseling is recommended.
Positive	Mutation Detected: del18bp (HT)	del18bp heterozygote (HT) - One copy of the del18bp (delPhe323Tyr328) mutation was identified indicating that this individual is a carrier for Torsion dystonia. This interpretation is based on the assumption that this individual is not clinically affected with Torsion dystonia. Genetic counseling is recommended.
Positive	Mutation Detected: delGAG (HM)	delGAG homozygote (HM) - Two copies of the delGAG mutation were identified indicating that this individual is affected by Torsion dystonia. Genetic counseling is recommended.
Positive	Mutation Detected: del18bp (HM)	del18bp homozygote (HM) - Two copies of the del18bp (delPhe323Tyr328) mutation were identified indicating that this individual is affected by Torsion dystonia. Genetic counseling is recommended.

Clinical Significance: Dystonia is a movement disorder involving sustained muscle contractions and abnormal posturing with a strong hereditary predisposition and without a distinct neuropathology. Torsion dystonia is a form of dystonia known as early-onset dystonia (also called idiopathic or generalized torsion dystonia) that begins in childhood around the age of 12. Torsion dystonia is an autosomal dominant condition, which means that dystonia appears when a person is heterozygous, having one copy of a mutated gene and one copy of a normal gene. Torsion dystonia has a 30% to 40% penetrance, meaning 30 to 40 percent of people who have a mutated gene develop symptoms. This disorder has been estimated to occur at rates approximately 5 to 10 fold greater in the Ashkenazi Jewish community, as compared to non-Jewish and non-Ashkenazi populations. A 3-bp (CAG) deletion in the coding region of the TOR1A (DYT1) gene, located on chromosome 9q34, accounts for the majority of cases with this form of dystonia, especially in individuals of Ashkenazi Jewish descent. A second mutation, 18-bp deletion (Phe323_Tyr328del) has recently been identified. The TOR1A gene, which encodes the protein, torsinA, is a member of a gene family with three homologous members in humans, encoding torsinB, torp2 (torp2a), and torp3 (torp3a). The precise function of torsinA is not known.