FRMD7 Gene Analysis in X-linked Congenital Nystagmus

Disorder also known as: Nystagmus congenital motor 1; X-linked infantile nystagmus 1; infantile idiopathic nystagmus (IIN); X-linked, infantile periodic alternating nystagmus (XLPAN).

Clinical Features:
X-linked congenital nystagmus is an X-linked hereditary form of congenital idiopathic nystagmus (CIN). The onset of nystagmus is during the infancy (less than 6 month of age). Congenital nystagmus typically presents with conjugate, horizontal oscillations of the eyes. Rarely the nystagmus is vertical or monocular. These oscillations usually occur during primary or eccentric gaze, often with an anomalous of the head posture head. Other features include strabismus, refractive error, and head movements.

Other disorders to be differentiated from CIN are: Acquired nystagmus; inner ear disorders such as labyrinthitis or Meniere's disease; toxic cause: drugs, medication, or alcohol intoxication; head injury; stroke or any disease of the brain.

Other inherited disorders associated with nystagmus: Albinism, achromatopsia, X-linked congenital stationary blindness, Leber congenital amaurosis, optic disc atrophy, optic nerve hypoplasia, and aniridia.

Inheritance Pattern/Genetics:
Prevalence rates of 1 in 1,000 to 1 in 1,500 have been reported for CIN.[4] CIN is genetically heterogeneous, with autosomal dominant, autosomal recessive and X-linked inherited forms of CIN have been described.

FRMD7-related CIN is inherited as X-linked trait and affects predominantly males. Nevertheless, depending on the degree of X-inactivation, up to 50% of carrier females are also affected.

Test Methods:
Using genomic DNA obtained from the submitted biological material, bi-directional sequence of the coding region and splice junctions of the 12 exons of the FRMD7 gene is analyzed to evaluate for a variant in this gene. Variants found in the first person of a family to be tested are confirmed by repeat analysis using sequencing, restriction fragment analysis, or another appropriate method.

Test Sensitivity:

FRMD7 is the only gene known to cause CIN. One study reports a sensitivity of full gene sequencing in affected individuals from families with two or more affected individuals of either gender to be approximately 57%.[3] This same study reported a sensitivity of approximately 7% for affected individuals with no family history but who had received a careful clinical evaluation.

References:

1. Mellot et al., (1999) Arch Ophthalmol 117:1630-33.
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3. Tarpey et al., (2006) Nat Genet 38:1242-1244.
4. Self J et al., (2007) Ophthalmic Genet 28(4):187-91.
5. Thomas MG et al., (2009) GeneReviews [Internet]. Seattle (WA): University of Washington, Seattle Feb 12.