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## **MYO7A Gene Test for Usher Syndrome Type I**

### **Background:**

Usher Syndrome represents the most common type of autosomal recessive syndromic hearing loss and is the most common genetic cause of combined deafness and blindness. Its prevalence is about 4/100,000 with an estimated carrier frequency of 1/70 (Boughman et al., 1983; Rosenberg et al, 1997). This syndrome is subdivided into three clinical types depending on the severity and onset of hearing impairment as well as the presence of a vestibular dysfunction. Usher Syndrome Type 1 is the most severe form that is characterized by congenital sensorineural hearing loss, vestibular dysfunction and an onset of retinitis pigmentosa by the age of ten (Kimberling, 2004). Because of the vestibular areflexia, infants have rarely learned to walk before the age of 18 months.

Pathogenic mutations in *MYO7A* gene are found in about 60% of patients with Usher Syndrome Type 1 (Kimberling, 2004). Identified disease causing mutations include missense, nonsense, frameshift, splice-site as well as deletions. They are distributed across nearly all exons, but the majority is clustered in the exons encoding the *MYO7A* motor domain. No genotype-phenotype correlations have been reported thus far.

*MYO7A* mutations have been reported in several families with recessive nonsyndromic hearing loss. In addition, a few families with autosomal dominant nonsyndromic hearing loss (DFNA11) have also been described with mutations in *MYO7A*.

**Synonyms:** USHER SYNDROME, TYPE IB

**Gene:** *MYO7A* (myosin VIIA)

**Protein:** myosin VIIA

**Location:** 11q13.5

**Epidemiology:** ~ 4/100,000 (Usher Types 1, 2 and 3)

- Both males and females are affected with equal frequency.
- Appears to be more common in the Acadian population of Louisiana and in Northern Sweden (Kimberling, 1995).

### **Clinical features:**

- Profound congenital deafness
- Vestibular problems (manifests as delayed walking >18 months)
- Progressive retinitis pigmentosa

**Inheritance pattern:** Autosomal recessive

- Parents of an affected child are unaffected but carry a single mutation in the gene.
- Parents that are both carriers of the *MYO7A* gene mutation have a 25% (or 1 in 4) risk of having an affected child.

**Test indications**

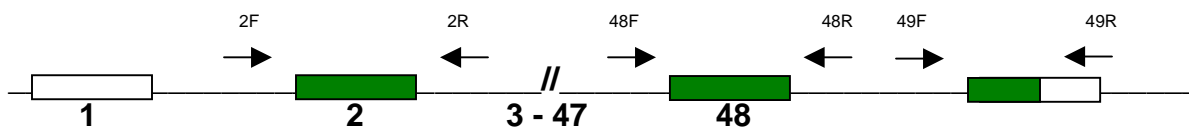
- Patients with clinical features associated with Usher Syndrome Type I:
  - Hearing loss that is severe-to-profound, bilateral and present at birth
  - Hearing loss associated with delayed walking
  - Hearing loss associated with absence of vestibular responses
  - Hearing loss associated with retinitis pigmentosa
- Prenatal testing if parents have a child with Usher Syndrome and an identified *MYO7A* mutations.

**Test outcome:**

- The detection of pathogenic mutations in both copies of the *MYO7A* gene is considered a positive test result.
- Identification of only one mutation in *MYO7A* gene in an affected individual is difficult to interpret. Some of these individuals might have Usher Syndrome due to another gene. Others may have a second pathogenic *MYO7A* mutation in a non-coding region of the gene that is not assessed by this test.

**Turn-around-time:** 5 weeks

**Methodology:** Bi-directional sequence analysis of 48 coding exons and their splice sites in the *MYO7A* gene. This test does not detect large deletions or mutations in non-coding regions that could potentially affect the expression of the gene.



**Sensitivity:** This assay is greater than 99.9% accurate in detecting mutations in the sequence analyzed. According to the literature, *MYO7A* mutations have been detected in about 60% of patients with Usher Syndrome Type I.

**Cost and CPT codes:**

Full sequencing of the gene

- Cost: \$1750
- CPT codes: 83891(1), 83894(1), 83898(46), 83904(46), 83912(1)

#### Testing for known familial mutation

- Cost: \$250
- CPT codes: 83891(1), 83894(1), 83898(1), 83904(1), 83912(1)

#### References:

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Rosenberg T, Haim M, Hauch AM, Parving A (1997) The prevalence of retinitis pigmentosa and other retinal dystrophy-hearing impairment associations. *Clin Genet* 51:314-321.

Tamagawa Y, Ishikawa K, Ishikawa K, Ishida T, Kitamura K, Makino S, Tsuru T, Ichimura (2002) Phenotype of DFNA11: a nonsyndromic hearing loss caused by a myosin VIIA mutation. *Laryngoscope* 112(2):292-7.