

Usher Syndrome Type 1 via *CDH23* Gene Sequencing -- Test #642

Brief Description of Clinical Features: Usher syndrome is a clinically heterogeneous disorder characterized by progressive retinitis pigmentosa (RP) and sensorineural hearing impairment, with or without vestibular abnormalities. Three types are recognized based on the age of onset, severity of symptoms and the vestibular involvement. **Usher syndrome type 1** (USH1 OMIM 276900) is the most common type. It is distinguished by congenital onset of hearing loss, RP in the first decade of life, and abnormal vestibular function (Cohen et al. Int J Audiol 46:82-93, 2007). Features of RP include night blindness progressing to constriction of the peripheral visual field with eventually loss of central vision, abnormal fundus with bone-spicule deposits/attenuated retinal vessels, and abnormal electroretinographic (ERG) findings (Daiger et al. Arch Ophthalmol 125:151-158, 2007). The vestibular abnormality results in development delay in sitting and walking. See also the American Speech-Language-Hearing Association (www.asha.org) and Keats and Lentz (GeneReviews, 2010, www.genetests.org).

Genetics: USH1 is a genetically heterogeneous autosomal recessive disease. Mutations in four genes: *MYO7A*, *CDH23*, *PCDH15*, and *USH1C* account for ~ 75% of cases with detectable mutations (Weil et al. Nature 374:60-61, 1995; Bork et al. Am J Hum Genet 68:26-37, 2001; Ahmed et al. Am J Hum Genet 69:25-34, 2001; Bitner-Glindzicz et al. Nat Genet 26:56-60, 2000; Keats and Lentz, 2010). Mutations in the *CDH23* gene account for up to 35% of the cases. About 100 *CDH23* causative mutations have been reported to date. The majority are missense, although nonsense, splicing and small insertion or deletion mutations have also been reported. In addition to USH1, about 30 missense *CDH23* mutations have been reported in patients with autosomal recessive nonsyndromic hearing loss (DFNB12 OMIM 601386) (Astuto et al. Am J Hum Genet 71:262-275, 2002; Shahin et al. Eur J Hum Genet 18:407-413, 2010).

Description of This Particular Test: The *CDH23* gene encodes cadherin, a cell adhesion protein. This test involves bidirectional DNA sequencing of all coding exons and splice sites of the *CDH23* gene. The full coding sequence of each exon plus ~ 50 bp of flanking DNA on either side are sequenced. As indicated, we will also sequence one (Test #100) or two (Test #200) exons in family members of patients with known mutations or to confirm previous results.

Reference Sequences: Genomic: **NC_000010.9** mRNA: **NM_002212.4** Protein: **NP_071407.4**

Indications for Test: All patients with symptoms suggestive of combined sensorineural hearing loss, RP and vestibular areflexia, and no mutations in *MYO7A*. The *CDH23* gene is also a candidate for patients presenting with DFNB12.

Sensitivity of Test: This test allows the detection of mutations in up to 35% of patients with USH1 (Keats and Lentz, 2010). PreventionGenetics offers a sequencing panel of the four genes that are frequently mutated in patients with USH1 patients (Test #645).

Turnaround Time: Maximum of 40 days, although many tests are completed in 2-3 weeks.

Specimen Requirements: See page 4 of the Requisition Form.

Price: **Sequencing of all *CDH23* Coding Exons** **\$ 2790**

CPT Codes:

Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1	83891 \$ 40
Amplification x70	83898 \$ 990	Sequencing x70	83904 \$1480
Separation x1	83894 \$ 110	Interpretation/Report x1	83912 \$ 140

Accreditation: CLIA ID #: **52D1027685** (expires 1/18/13) (CAP#: 7185561, AU ID: 1407125 expires 12/20/12)

Contact: Dr. Khemissa Bejaoui, khemissa@preventiongenetics.com, www.preventiongenetics.com