

## Usher Syndrome Type 1 via *PCDH15* Gene Sequencing -- Test #644

**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](http://www.asha.org)) and Keats and Lentz (GeneReviews, 2010, [www.genetests.org](http://www.genetests.org)).

**Genetics:** USH1 is an autosomal recessive disease that is genetically heterogeneous. 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 *PCDH15* gene account for about 19% of the cases. Over 30 *PCDH15* causative mutations have been reported. They include nonsense, splicing, small insertions or deletions, and three large deletions. In addition to USH1, *PCDH15* mutations have been reported in patients with autosomal recessive non-syndromic hearing loss (DFNB23, OMIM 609533) (Ahmed et al. Hum Mol Genet 12:3215-3223, 2003).

**Description of This Particular Test:** The *PCDH15* gene encodes protocadherin15, a cell adhesion protein that is important in the development of neurosensory cells in the retina and cochlea. This test involves bidirectional DNA sequencing of all coding exons and splice sites of the *PCDH15* gene. The full coding sequence of each exon plus ~ 50 bp of flanking DNA on either side are sequenced. As indicated, we will sequence one (Test #100) or two (Test #200) exons in family members of patients with known mutations or to confirm previous results (\$190-\$340).

**Reference Sequences:** Genomic: NC\_000010.9 mRNA: NM\_033056.3 Protein: NP\_149045.3 (CCDS 7248.1)

**Indications for Test:** All patients with symptoms suggestive of combined neurosensory hearing loss, RP and vestibular areflexia, and no mutations in *MYO7A* or *CHD15*. The *PCDH15* gene is also a candidate for patients presenting with DFNB23.

**Sensitivity of Test:** This test allows the detection of mutations in ~19% of patients with USH1 (Keats and Lentz, 2010).

**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 *PCDH15* Coding Exons \$ 1710

**CPT Codes:**

Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1	83891 \$ 40
Amplification x38	83898 \$ 570	Sequencing x38	83904 \$ 850
Separation x1	83894 \$ 90	Interpretation/Report x1	83912 \$ 130

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

**Contact:** Dr. Khemissa Bejaoui, [khemissa@preventiongenetics.com](mailto:khemissa@preventiongenetics.com), [www.preventiongenetics.com](http://www.preventiongenetics.com)