

Usher Syndrome via Sequential Sequencing of MYO7A, CDH23, PCDH15 and USH1C Genes -- Test #645

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.

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). About 350 different causative mutations were detected in the four genes that are most frequently mutated in USH1 patients (www.genetests.org). See also individual gene Test Descriptions.

Description of These Tests: PreventionGenetics offers sequencing of each of the four genes individually, or the sequential Panel described here. These tests involve bidirectional DNA sequencing of all coding exons of the genes as well as ~50 bp of flanking DNA on either side.

Reference Sequences:

Gene	<i>MYO7A</i>	<i>CDH23</i>	<i>PCDH15</i>	<i>USH1C</i>
Genomic NC_	000011.8	000010.9	000010.9	000011.8
mRNA NM_	000260.3	0022124.4	033056.3	153676.3
Protein NP_	000251.3	071407.4	149045.3	710142.1
CCDS	NA	NA	7248.1	7825.1
Sensitivity	39-55%	19-35%	11-19%	6-7%

Indications for Test: Patients with combined congenital sensorineural hearing loss, RP and vestibular areflexia.

Sensitivity of Test: Together, these four tests may detect mutations in up to 75% of all USH1 patients (see table above; Keats and Lentz, 2010).

Turnaround Time: Maximum of 60 days.

Specimen Requirements: See page 4 of the Requisition Form

Prices and CPT Codes:

CPT	Description	<i>MYO7A Only</i>	<i>CDH23 Only</i>	<i>PCDH15 Only</i>	<i>USH1C Only</i>	<i>All Four Genes</i>
83890	Sample Ascertainment	\$ 30 (x1)	\$ 30 (x1)	\$ 30 (x1)	\$ 30 (x1)	\$ 30 (x1)
83891	DNA Isolation	\$ 40 (x1)	\$ 40 (x1)	\$ 40 (x1)	\$ 40 (x1)	\$ 40 (x1)
83898	Amplification	\$ 700 (x48)	\$ 990 (x70)	\$ 570 (x38)	\$ 430 (x27)	\$ 2430 (x183)
83904	Sequencing	\$ 1050 (x48)	\$ 1480 (x70)	\$ 850 (x38)	\$ 640 (x27)	\$ 3640 (x183)
83894	Separation	\$ 100 (x1)	\$ 110 (x1)	\$ 90 (x1)	\$ 70 (x1)	\$ 320 (x1)
83912	Interpretation/Report	\$ 140 (x1)	\$ 140 (x1)	\$ 130 (x1)	\$ 110 (x1)	\$ 230 (x1)
	Totals	\$ 2060	\$ 2790	\$ 1710	\$ 1320	\$ 6690

When three genes are sequenced, the total cost will be discounted 15%.

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