

## Joubert Syndrome Gene Sequencing Panel (Test #294)

**Brief Description of Clinical Features:** Joubert syndrome (JS) (OMIM 213300) is marked by hypotonia, abnormal ocular movements, neonatal respiratory difficulties, mental retardation, hypoplasia of the cerebellar vermis, and malformation of the brainstem. The brain malformations lead to the "molar tooth sign" on cranial MRI, which is the hallmark clinical feature of JS. Other variable JS features include cystic kidneys, nephronophthisis, retinal dystrophy, ocular coloboma, occipital encephalocele, polydactyly, ataxia, and hepatic fibrosis. For more information, see Parisi and Glass (Gene Reviews, www.genetests.org, 2007; Parisi et al. Eur J Hum Genet 15:511-521, 2007).

JS clinical features overlap with a group of diseases known as ciliopathies, which include Meckel-Gruber syndrome (MKS) (OMIM# 249000), Joubert syndrome, Bardet-Biedl syndrome (BBS) (OMIM# 209900), Nephronophthisis (OMIM 256100), Senior-Loken syndrome (OMIM# 609294) and Leber congenital amaurosis (LCA). For more information, see Hildebrandt et al. J Am Soc Nephrol 20:23-35, 2009.

**Genetics:** The Ciliopathies exhibit autosomal recessive inheritance. All Ciliopathies have high levels of locus heterogeneity. Ciliopathies are caused by mutations in genes encoding proteins involved in cilia/centrosome structure, maintenance or function (Hildebrandt et al. 2009). These disorders may represent a phenotypic continuum of a single clinical entity.

**Description of This Particular Test:** The following genes will be tested in the order specified in the Table below, unless a different order is requested by the client. Please note that an Ashkenazi Jewish founder mutation has been reported in the *TMEM216* gene (Edvardson et al. Am J Hum Genet 86:93-97, 2010). Testing is accomplished by amplifying and sequencing the coding exons and ~50 bp of adjacent non-coding sequence. See also the individual Test Descriptions for each gene.

### Reference Sequences:

Gene	Disease	Genomic: NC	mRNA: NM	Protein: NP	CCDS:
<i>AHI</i>	JS	000006.11	017651.3	060121.3	47483.1
<i>TMEM67</i>	JS and MKS	000008.9	153704.4	714915.3	
<i>CEP290</i>	JS and MKS	000012.11	025114.3	079390.3	
<i>NPHP1</i> deletion	JS	000002.10	000272.2	000263.2	2086.1
<i>CC2D2A</i>	JS and MKS	000004.10	001080522.2	001073991.2	
<i>RPGRIP1L</i>	JS and MKS	000016.8	015272.2	056087.2	
<i>INPP5E</i>	JS	000009.11	019892.3	063945.2	7000.1
<i>ARL13B</i>	JS	000003.10	182896.1	878899.1	2925.1
<i>TMEM216</i>	JS	000011.9	016499.3	057583.2	

**Indication for Testing:** Candidates for this test are patients with symptoms consistent with JS.

**Sensitivity of Test:** Sensitivity for JS testing is at least 50% overall

**Turnaround Time:** Maximum of 100 days.

**Specimen Requirements:** See page 4 of the Requisition Form.

### CPT Codes and Prices

Codes	<i>AHI</i>	<i>TMEM67</i>	<i>CEP290</i>	<i>NPHP1</i> Deletion	<i>CC2D2A</i>	<i>RPGRIP1L</i>	<i>INPP5E</i>	<i>ARL13B</i>	<i>TMEM216</i>	Panel
83890	\$ 30	\$ 30	\$ 30	\$ 30	\$ 30	\$ 30	\$ 30	\$ 30	\$ 30	\$ 30
83891	\$ 40	\$ 40	\$ 40	\$ 40	\$ 40	\$ 40	\$ 40	\$ 40	\$ 40	\$ 40
83898	\$410	\$380	\$ 755	\$ 50	\$530	\$380	\$190	\$170	\$110	\$3000
83904	\$670	\$670	\$1245	\$ 00	\$790	\$580	\$290	\$260	\$160	\$4440
83894	\$ 60	\$ 60	\$ 40	\$ 90	\$ 80	\$ 70	\$ 50	\$ 60	\$ 40	\$400
83912	\$110	\$ 110	\$ 80	\$ 80	\$ 120	\$ 90	\$ 90	\$ 80	\$ 80	\$300
<b>Totals:</b>	<b>\$1320</b>	<b>\$1290</b>	<b>\$2190</b>	<b>\$290</b>	<b>\$1590</b>	<b>\$1190</b>	<b>\$690</b>	<b>\$640</b>	<b>\$460</b>	<b>\$8210*</b>

\* When five or more of the genes are sequentially tested, 15% discount will apply to the total cost of the tests.

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

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