

## Joubert Syndrome via *TMEM216* Gene Sequencing (Test #291)

**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](http://www.genetests.org), 2007) and Parisi et al. (Eur J Hum Genet 15:511-521, 2007).

**Genetics:** JS is inherited in an autosomal recessive manner. Recently an Ashkenazi Jewish founder mutation was identified in the *TMEM216* gene as a new cause of JS (Edvardson et al. Am J Hum Genet 86:93-97, 2010). Additional families from other ethnicities have also been linked to the JBTS2 region, which harbors *TMEM216*. Other cases of JS have also been linked to mutations in the *AH11*, *CEP290*, *TMEM67/MKS3*, *RPGRIP1L*, *INPP5E*, *ARL13B* and *NPHP1* genes. PreventionGenetics performs tests for all of these genes.

**Description of This Particular Test:** This test involves bidirectional sequencing using genomic DNA of all five exons (exons 1-5) of the *TMEM216* gene. The full coding region of each exon plus ~50 bp of flanking non-coding DNA on each side are sequenced. We will also perform sequencing of any single exon or pair of exons for family members of patients with known mutations and to confirm previous results (\$190-340 charge).

**To support research and because development of this test was funded by the NIH, a completed Clinical Feature Checklist, which is available from our web site, must accompany each test requisition. Checklists are not required for carrier testing.**

**Indications for Test:** Candidates for this test are patients with symptoms consistent with JS and the family members of patients who have known mutations. Conclusive connections between clinical features and mutated genes have not yet been made for JS. This test should be performed first for patients with Ashkenazi Jewish ancestry.

**Sensitivity of Test:** The prevalence of JS is approximately 1 in 100,000. The following are the *approximate* fractions of patients with mutations in the indicated genes for Joubert syndrome: *TMEM67/MKS3* 10%, *AH11* 10%, *CC2D2A* 10%, *CEP290* 10%, *RPGRIP1L* 2%, *ARL13B* 2%, *NPHP1* 2%.

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

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

<b>Price:</b>	<b>Sequencing of <i>TMEM216</i> gene</b>	<b>\$ 460</b>
<b>CPT Codes:</b>		
Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1 83891 \$ 40
Amplification x5	83898 \$110	Sequencing x5 83904 \$160
Separation x1	83894 \$ 40	Interpretation/Report x1 83912 \$ 80

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

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