### Joubert Syndrome: Sequencing Panel

**Test Code:** MM136  
**Turnaround time:** 6 weeks  
**CPT Codes:** 81406 x1

#### Condition Description

Joubert syndrome (JS) is an autosomal recessive multisystem disease characterized by cerebellar vermis hypoplasia with prominent superior cerebellar peduncles (resulting in the 'molar tooth sign', or MTS, on axial MRI), intellectual disability, hypotonia, irregular breathing pattern, and eye movement abnormalities. Some individuals with JS have retinal dystrophy and/or progressive renal failure characterized as nephropathisis. The disorder in such patients is referred to as cerebellooculo renal syndrome, or CORS. Individuals with a mild form of JS have been shown to have a homozygous deletion of the NPHP1 gene identical, by mapping, to that in subjects with nephropathisis alone. Please note, the *CEP164* gene is not included in the NGS panel at this time due to presence of at least one pseudogene. For clinicians that would like *CEP164* analysis in the event that all other genes test negative, we request that you contact EGL directly. Please note, the *TMEM138* and *TMEM231* genes are not included on the NGS panel at this time as these genes are only partially annotated in hg19. *TMEM138* and *TMEM231* will be re-evaluated with the release of hg20.

#### References:
- OMIM  
- GeneReviews

#### Genes

*AH1*, *ARL13B*, *C5orf42*, *CC2D2A*, *CEP290*, *CEP41*, *KIF7*, *NPHP1*, *QFD1*, *RPGRIP1L*, *TCTN1*, *TCTN2*, *TCTN3*, *TMEM16*, *TMEM216*, *TMEM67*, *TTQ218*, *ZNF423*

#### Indications

This test is indicated for:
- Confirmation of a clinical diagnosis of Joubert syndrome.  
- Carrier testing in adults with a family history of Joubert syndrome.

#### Methodology

**Next Generation Sequencing:** In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

#### Detection

**Clinical Sensitivity:** Unknown. Pathogenic variants in the promoter region, some pathogenic variants in the introns and other regulatory element pathogenic variants cannot be detected by this analysis. Large deletions will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical and/or biochemical phenotype.  
**Analytical Sensitivity:** ~99%

#### Specimen Requirements

Submit only 1 of the following specimen types

**Type: Whole Blood**

Specimen Requirements:
- In EDTA (purple top) tube:  
  - Infants (2 years): 3-5 ml  
  - Older Children & Adults: 5-10 ml
- Specimen Collection and Shipping: Ship sample at room temperature with overnight delivery.

**Type: Isolated DNA**

Specimen Requirements:
- In microtainer: 60 ug
Isolation using the Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping: Refrigerate until time of shipment in 100 ng/ul of TE buffer. Ship sample at room temperature with overnight delivery.

**Special Instructions**

Please include fundus photographs, electroretinogram (ERG) findings, visual field findings, and visual acuity, if available, for expert review and clinical correlation with test results.

**Related Tests**

- Eye Disorders: Comprehensive Sequencing and Deletion/Duplication Panels
- Joubert Syndrome: Deletion/Duplication Panel