### Condition Description

Many genes are associated with Mendelian forms of malformations of brain development. Genes involved in the malformations in the brain show locus heterogeneity and have been typically identified in small kindred sizes. Therefore, the diagnostic classifications can be difficult and may not reflect the molecular pathogenesis. Pathogenic variants have been detected in more than 51 genes and are known to cause lissencephaly, cerebellar hypoplasia disorders, and Joubert syndrome. These disorders can be inherited in an autosomal dominant, autosomal recessive, or X-linked manner.

Note: This test does not detect the retrotransposon insertion in the 3' UTR of the FKTN gene common in some Asian populations. For patients with suspected Fukuyama congenital muscular dystrophy, testing for the FKTN insertion is recommended. Analysis for the FKTN insertion is available as a separate assay.

References:


### Genes

ACTB, ACTG1, ADGRC1, AHI1, ARFGGEF2, ARX, CASK, CC2D2A, CEP290, CEP41, CHMP1A, DCX, EOMES, EXOSC3, FKRP, FKTN, FLNA, KIF1BP, KIF7, LAMC3, LARGE1, MKS1, NPHP1, OPHN1, PAFAH1B1, POMGRN1, POMT1, POMT2, PQBP1, RAB3GAP1, RAB3GAP2, RARS2, RELN, RGGRIP1L, RTTN, SRPX2, TMEM138, TMEM216, TMEM237, TMEM267, TSEN2, TSEN34, TSEN54, TUBA1A, TUBA8, TUBB2B, TUBB3, VLDLR, VRK1, WDR62

### Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of a brain malformation.

### 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

**Next Generation Sequencing**: 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.

**Related Tests**

- Brain Malformations: Deletion/Duplication Panel