PAFAH1B1-associated Lissencephaly/Subcortical Band Heterotopia: PFAH1B1 Gene Deletion/Duplication

Test Code: DPFA
Turnaround time: 2 weeks
CPT Codes: 81405 x1

Condition Description

PAFAH1B1-associated lissencephaly/subcortical band heterotopia (SBH) includes Miller-Dieker syndrome (MDS) and isolated lissencephaly sequence (ILS). During embryogenesis, reduced levels of neuronal migration cause the cortical malformations, lissencephaly and SBH. Lissencephaly refers to a "smooth brain" with absent gyri or abnormally wide gyri. SBH refers to a band of heterotopic gray matter located beneath the cortex but separated from it by a thin layer of normal white matter. MDS is characterized by lissencephaly, distinctive facial features, and severe neurological abnormalities. ILS is characterized by lissencephaly, which leads to developmental delay, intellectual disability, and seizures.

Mutation of the PFAH1B1 (17p13.3) gene, previously known as the LIS1 gene, cause PFAH1B1-associated lissencephaly/subcortical band heterotopia. MDS is caused by deletions that include both the PFAH1B1 and the YWHAE genes. ILS is caused by mutation of the PFAH1B1 gene with ~68% of mutations being detected by deletion/duplication analysis and ~32% being detected by sequencing analysis.

Please note that lissencephaly and SBH are graded by anterior-posterior gradient and severity. When the lissencephaly or SBH is more severe posteriorly, it is referred to as a posterior to anterior (p>a) gradient. When more severe anteriorly, it is referred to as an anterior to posterior (a>p) gradient. PFAH1B1 abnormalities generally give rise to a p>a gradient, whereas abnormalities of DCX generally give rise to an a>p gradient (GeneReviews). This testing is for the PFAH1B1 gene only.

For patients with suspected PFAH1B1-associated lissencephaly/subcortical band heterotopia, deletion/duplication analysis is recommended as the first step in mutation identification. For patients in whom mutations are not identified by deletion/duplication analysis, full gene sequencing is appropriate.

References:
- GeneReviews
- OMIM #601545: PFAH1B1 gene
- OMIM #607432: Lissencephaly 1

Deletion/Duplication testing should be ordered as the first tier test.

Genes

LIS1, PFAH1B1

Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of PFAH1B1-Associated Lissencephaly/Subcortical Band Heterotopia.
- Carrier testing in adults with a family history of PFAH1B1-Associated Lissencephaly/Subcortical Band Heterotopia.

Methodology

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region.

Detection

100% of MDS will be detected by deletion/duplication analysis. 68% of ILS will be detected by deletion/duplication analysis. Detection is limited to duplications and deletions. The CGH array will not detect point or intronic mutations. Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

Specimen Requirements

Submit only 1 of the following specimen types

Type: Whole Blood (EDTA)

Specimen Requirements:
EDTA (Purple Top)
Infants and Young Children (2 years of age to 10 years old): 3-5 ml
Older Children & Adults: 5-10 ml
Autopsy: 2-3 ml uncotted cord or cardiac blood
Specimen Collection and Shipping:
Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

**Type: DNA, Isolated**

**Specimen Requirements:**
Microtainer
3µg
Isolation using the Perkin Elmer™Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

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

**Related Tests**

- Sequence analysis of the *PAFAH1B1* gene is available for those individuals in whom deletion/duplication analysis is negative.
- Both sequencing (SO) and deletion/duplication (SQ) analysis of the *DCX* gene is available.
- Custom diagnostic mutation analysis (KM) is available to family members if mutations are identified by targeted mutation testing or sequencing analysis.
- Prenatal testing is available only for known familial mutations to individuals who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.