Pitt-Hopkins-like Syndrome-2: NRXN1 Gene Deletion/Duplication

Condition Description

Pitt-Hopkins-like syndrome-1 and Pitt-Hopkins-like syndrome-2 are inherited in an autosomal recessive manner and are caused by mutations in the CNTNAP2 (7q35) and NRXN1 (2p16.3) genes respectively. Both of these conditions resemble Pitt-Hopkins syndrome, caused by mutation of the TCF4 gene, with regard to the distinctive facial features, severe intellectual disability and breathing abnormalities; however, there is a phenotypical difference. While speech is severely impaired, individuals with mutation the CNTNAP2 or NRXN1 gene have normal or mildly delayed motor milestones.

Please note that this test is for the NRXN1 gene only.

For patients with suspected Pitt-Hopkins-like syndrome-2, sequence analysis is recommended as the first step in mutation identification. For patients in whom mutations are not identified by full gene sequencing, deletion/duplication analysis is appropriate.

References:

- OMIM #600565: NRXN1 gene
- OMIM #610954: PTHS

Genes

NRXN1

Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of Pitt-Hopkins-like syndrome-2 in an individual in whom sequence analysis was negative.
- Carrier testing in adults with a family history of Pitt-Hopkins-like syndrome-2 in whom sequence analysis was negative.

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

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 unclotted 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 3ug
- Isolation using the Perkin Elmer™Chemagen™ 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.

**Special Instructions**

Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of EGL Genetics, please submit a copy of the sequencing report with the test requisition.

**Related Tests**

- Sequence analysis of the NRXN1 gene is available and is required before deletion/duplication analysis.
- Sequencing and deletion/duplication analysis of the CNTNAP2 and TCF4 genes are 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.