Neurodegeneration due to Cerebral Folate Transport Deficiency: *FOLR1* Gene Deletion/Duplication

**Test Code:** DFOLR  
**Turnaround time:** 2 weeks  
**CPT Codes:** 81228 x1

### Condition Description

Loss-of-function mutations in the *FOLR1* gene (11q13.4) cause an inherited disorder of brain-specific folate deficiency. The *FOLR1* gene encodes the folate receptor alpha (FRα), one of two GPI-anchored receptors that mediate cellular uptake of 5-methyltetrahydrofolate (MTHF). Mutations in the *FOLR1* gene impair the cerebral folate transport function. Features of this autosomal recessive disorder begin in late infancy and include severe developmental regression, movement disturbances, epilepsy, and leukodystrophy.

For patients with suspected neurodegeneration due to cerebral folate transport deficiency, 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 #613068: Neurodegeneration due to cerebral folate transport deficiency
- OMIM #136430: *FOLR1* gene

### Genes

*FOLR1*

### Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of neurodegeneration due to cerebral folate transport deficiency in an individual in whom sequence analysis was negative.
- Carrier testing in adults with a family history of neurodegeneration due to cerebral folate transport deficiency 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: 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.

**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.
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 FOLR1 gene is available and is required before deletion/duplication analysis.
- 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.