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.

Please note that a “backbone” of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient's phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

### 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

* Preferred specimen type: Whole Blood

**Type: Whole Blood**

Specimen Requirements:
- In EDTA (purple top) or ACD (yellow top) tube:  
  - Infants (2 years): 3-5 ml  
  - Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Type: Saliva**
Specimen Requirements:

Oragene\textsuperscript{TM} Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection 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 Emory Genetics Laboratory, please submit a copy of the sequencing report with the test requisition.

Related Tests

- Sequence analysis of the \textit{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.