## Condition Description

Formiminotransferase deficiency is an autosomal recessive disorder that is the second most common inborn error of folate metabolism. There are two forms of the disorder: a severe phenotype and a mild phenotype. The severe phenotype is associated with elevated levels of formiminoglutamate (FIGLU) in the urine in response to histidine administration, megaloblastic anemia, and mental retardation. Features of the mild phenotype include high urinary excretion of FIGLU in the absence of histidine administration, mild developmental delay, and no hematological abnormalities.

Formiminotransferase-cyclodeaminase (FTCD) is a bifunctional enzyme that catalyzes two consecutive reactions that couple histidine degradation to folate metabolism. The highest levels of FTCD are found in the liver. While high levels of FIGLU in the urine suggest FTCD deficiency, there are other causes of elevated FIGLU excretion. Confirmation of a diagnosis of FTCD deficiency requires an enzyme assay from a liver biopsy; enzymatic activity is not detectable in either fibroblasts or blood cells. Mutations in the FTCD gene (21q22.3) cause formiminotransferase deficiency.

## Sources

(3) OMIM entries 229100 and 606806

## Genes

FTCD

## Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of FTCD deficiency in individuals who have tested negative for sequence analysis
- Carrier testing in adults with a family history of FTCD deficiency who have tested negative for sequence analysis

## 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) 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™ 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

Submit copies of diagnostic biochemical test results with the sample, if appropriate. Contact the laboratory if further information is needed.

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 \textit{FTCD} gene is available and is required before deletion/duplication analysis.
- Prenatal testing is available to couples who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.