Formiminotransferase Deficiency/FIGLU-uria: *FTCD* Gene Sequencing

**Test Code:** ZK  
**Turnaround time:** 4 weeks  
**CPT Codes:** 81479 x1

## 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:
- Individuals with a clinical and biochemical diagnosis consistent with *FTCD* deficiency.  
- Carrier testing in individuals with a family history of *FTCD* deficiency.

## Methodology

PCR amplification of 14 exons contained in the *FTCD* gene is performed on the patient's genomic DNA. Direct sequencing of amplification products is performed in both forward and reverse directions, using automated fluorescence dideoxy sequencing methods. The patient's gene sequences are then compared to a normal reference sequence. Sequence variations are classified as mutations, benign variants unrelated to disease, or variations of unknown clinical significance. Variants of unknown clinical significance may require further studies of the patient and/or family members. This assay does not interrogate the promoter region, deep intronic regions, or other regulatory elements, and does not detect large deletions.

## Detection

**Clinical Sensitivity:** Unknown  
**Analytical Sensitivity:** ~99%.

Mutations in the promoter region, some mutations in the introns, other regulatory element mutations, and large deletions cannot be detected by this analysis.

Results of molecular analysis should be interpreted in the context of the patient's 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

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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**

Please submit copies of diagnostic biochemical test results along with the sample. Contact the laboratory if further information is needed.

**Related Tests**

- Known Mutation Analysis (KM) is available to family members if mutations are identified by sequencing.
- Prenatal testing is available to individuals who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.