**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**

**Type: Saliva**

**Specimen Requirements:**
Oragene™ Saliva Collection Kit  
Oragene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

**Specimen Collection and Shipping:**  
Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

**Type: DNA, Isolated**

**Specimen Requirements:**
Microtainer  
8µg  
Isolation using the Perkin Elmer™Chemagen™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is
**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 24 hours of collection. Do not refrigerate or freeze.

**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.