Fukuyama Congenital Muscular Dystrophy: FKTN Gene Sequencing

Test Code: SFKTN
Turnaround time: 4 weeks
CPT Codes: 81405 x1

Condition Description

The congenital muscular dystrophies are a group of genetically and clinically heterogeneous hereditary myopathies characterized by congenital hypotonia and muscle weakness, contractures, and delayed motor development. Muscle biopsy usually reveals a nonspecific dystrophic pattern. The clinical course is broadly variable and can involve the brain and eyes. Initial testing often includes clinical evaluation, muscle imaging, electromyography, and muscle biopsy, followed by targeted genetic testing.

Fukuyama congenital muscular dystrophy (FCMD) was first described in 1960 and represents one if the most common autosomal recessive disorders in the Japanese population. FCMD is a severe CMD that is associated with mental retardation. Characteristics include hypotonia, symmetrical generalized muscle weakness, and CNS migration disturbances. The average occurrence of heterozygous carriers identified in various regions of Japan is one in 188.

Mutation of the FKTN gene (9q31) causes FCMD which is mostly found in the Japanese population. Approximately 80% of affected individuals of Japanese ancestry are homozygous for the founder mutation (a 3kb retrotransposonal insertion into the 3' UTR), while an additional 15-20% are compound heterozygotes for the founder mutation and another point mutation. The average occurrence of heterozygous carriers identified in various regions of Japan is one in 188.

NOTE: For patients with suspected FCMD, sequence analysis for the Japanese founder mutation is recommended as the first step in mutation identification. This insertion is not part of this sequencing test but is available as a separate assay.

References

- Bonnemann, Carsten. Personal communication, July 8, 2009.

Genes

FKTN

Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of Fukuyama CMD
- Carrier testing in adults with a family history of Fukuyama CMD

Methodology

PCR amplification of 9 exons contained in the FKTN 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 deoxy 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. Large deletions are not detected by this analysis. Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

Evaluation of the 3kb insertion is not done as part of this test.
## Detection

Clinical Sensitivity: Approximately 80% of affected individuals of Japanese ancestry are homozygous for the founder mutation, while an additional 15-20% are compound heterozygotes for the founder mutation and another point mutation. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's biochemical phenotype.

Analytical Sensitivity: ~99%

## Specimen Requirements

### Submit only 1 of the following specimen types

#### 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.

#### 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™ 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.

## 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

- Deletion/duplication analysis of the *FKTN* gene by CGH array is available for those individuals in whom sequence analysis is negative.
- Familial mutation testing is available to family members if mutations are identified by targeted mutation testing or sequencing 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.