Bethlem Myopathy/Ullrich Congenital Muscular Dystrophy: COL6A3 Gene Deletion/Duplication

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.

The collagens are a superfamily of extracellular matrix proteins that play a role in maintaining the integrity of various tissues. Collagen VI forms a microfibrillar network in close association with the basement membrane around muscle cells. Collagen VI is composed of three different peptide chains alpha1(VI), alpha2(VI), and alpha3(VI). The alpha1(VI) and alpha2(VI) chains are encoded by two genes -- COL6A1 and COL6A2 respectively -- situated on chromosome 2q37. COL6A3, the gene for the alpha3(VI) chain, maps to chromosome 2q37. Mutations in the type VI collagen genes are associated with Bethlem myopathy and Ullrich congenital muscular dystrophy, which are likely different ends of a clinical spectrum. Mutations are identified in approximately 66% of patients, with 60% affected in one condition and 40% affected in the other.

Methods

This test is indicated for:

- Confirmation of a clinical diagnosis of Bethlem myopathy or Ullrich CMD in an individual in whom sequencing analysis was negative.
- Carrier testing in adults with a family history of autosomal recessive Ullrich CMD in whom sequencing analysis was negative.

References

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 **COL6A3** is required before deletion/duplication analysis
- Analysis of the **COL6A1** and **COL6A2** genes is also available.
- 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.