Borjeson-Forssman-Lehmann Syndrome: *PHF6* Gene Deletion/Duplication

**Condition Description**

Borjeson-Forssman-Lehmann syndrome (BFLS) is an X-linked intellectual disability syndrome. Characteristics of this syndrome include severe mental defect, epilepsy, hypogonadism, hypometabolism, marked obesity, swelling of subcutaneous tissue of face, narrow palpebral fissure, and large but not deformed ears. Affected individuals may have a characteristic facial appearance consisting of prominent superciliary ridges, deep-set eyes, ptosis, and large ears.

The phenotype of BFLS seems to evolve with age. Generally, babies with BFLS are floppy, with failure to thrive, big ears, and small external genitalia. In childhood, boys may display learning problems and moderate short stature, with emerging truncal obesity and gynecomastia. Head circumference is usually normal, and macrocephaly may be seen. Big ears and small genitalia remain. Thethoes are short and fingers tapered and malleable. In late adolescence and adulthood, the classically described heavy facial appearance emerges.

Some heterozygous females display milder clinical features such as tapering fingers and shortened toes. Significant learning problems have been reported in approximately 20% of female carriers, and skewed X inactivation in approximately 95%. Carrier females have also been reported with epilepsy, characteristic facial features, obesity, amenorrhea, and hypothyroidism.

Mutations in the *PHF6* gene (Xq26.3) have been associated with BFLS.

**Click here** for the OMIM summary on this condition.

**Genes**

*PHF6*

**Indications**

This test is indicated for:

- Confirmation of a clinical/biochemical diagnosis of Borjeson-Forssman-Lehmann syndrome in individuals who have tested negative for sequence analysis
- Carrier testing in adult females with a family history of Borjeson-Forssman-Lehmann syndrome 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.

**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*

**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: DNA, Isolated**

**Specimen Requirements:**

Microtainer
- 3µg

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**

- Sequencing analysis of the *PHF6* gene is available (YH) and is required before deletion/duplication analysis.
- ACGH array-based test for deletion/duplication analysis of 64 different X-linked intellectual disability genes is available (OL).
- Prenatal testing is available to adult females who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.