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

Test Code: Y1
Turnaround time: 2 weeks
CPT Codes: 81228 x1

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. The toes are short and fingers tapered and malleable. In late adolescence and adult life, 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.

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. 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**

- Sequencing analysis of the *PHF6* gene is available (YH) and is required before deletion/duplication analysis.
- A CGH 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.