BCOR-related Disorders: BCOR Gene Sequencing

Test Code: SBCOR
Turnaround time: 6 weeks
CPT Codes: 81479 x1

Condition Description

Lenz microphthalmia syndrome
Lenz microphthalmia syndrome (LMS) is an X-linked disorder characterized by unilateral or bilateral microphthalmia and/or anophthalmia. Extraocular malformations may affect the ears, teeth, fingers, skeleton, and genitourinary system. Other features can include glaucoma, coloboma, hearing loss, microcephaly, webbed neck, and cleft lip/palate. Developmental delay or intellectual disability is present in approximately 60% of affected males. BCOR is the only gene known to be associated with LMS although another X-linked locus is also known to be associated. Female carriers are typically not affected.

Oculofaciocardiodental syndrome
Oculofaciocardiodental (OFCD) syndrome (OMIM #300166) is also associated with mutations in BCOR. OFCD syndrome affects females and is lethal in males. Characteristics include congenital cataracts with or without unilateral/bilateral microphthalmia, long narrow face, cleft palate, cardiac defects, and dental anomalies. Microphthalmia is less severe in OFCD syndrome than in LMS. Females with OFCD syndrome often have normal intelligence. Known BCOR mutations causing OFCD include point mutations, small deletions, and deletions involving one or more exons.

For patients with suspected BCOR-related disorders, sequence analysis is recommended as the first step in mutation identification. For patients in whom mutations are not identified by full gene sequencing, deletion/duplication analysis is appropriate.

References:
- GeneReviews
- OMIM #300166: OFCD Syndrome
- OMIM # 300485: BCOR gene

Genes

BCOR

Indications

This test is indicated for:
- Confirmation of a clinical diagnosis of a BCOR-related disorder.
- Carrier testing in adults with a family history of a BCOR-related disorder.

Methodology

Next Generation Sequencing: In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

Detection

Clinical Sensitivity: Unknown. 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 clinical and/or biochemical phenotype.

Analytical Sensitivity: ~99%

Specimen Requirements

Submit only 1 of the following specimen types
* Preferred specimen type: Whole Blood

Type: Whole Blood

Specimen Requirements:
In EDTA (purple top) or ACD (yellow 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.

**Related Tests**

- Deletion/duplication analysis of the *BCOR* gene by CGH array is available for those individuals in whom sequence analysis is negative.
- Custom diagnostic mutation analysis (KM) is available to family members if mutations are identified by targeted mutation testing or sequencing analysis.
- Prenatal testing is available only for known familial mutations to individuals who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.
- X-Linked Intellectual Disability panels are available for 30, 60, and 90 genes.