**BEST1-related Disorders: BEST1 Gene Deletion/Duplication**

**Condition Description**

Pathogenic variants in the BEST1 gene (11q12), also known as VMD2, have been associated with several ocular phenotypes. The BEST1 gene encodes the bestrophin-1 protein, which is expressed in the retinal pigment epithelium and has also been detected in the kidney, brain, spinal cord, and testis. The most common BEST1-related disorder is best vitelliform macular dystrophy (BVMD). Pathogenic variants in the BEST1 gene cause several clinically distinct disorders.

**Best Vitelliform Macular Dystrophy (BVMD)**

BVMD is a slowly progressive macular dystrophy that is inherited in an autosomal dominant manner. Onset is typically in childhood. Individuals with BVMD present with decreased central visual acuity and metamorphopsia. They retain normal dark adaptation and peripheral vision. Inter- and intrafamilial variability is seen regarding severity of vision loss and age of onset. The abnormalities observed in BVMD are restricted to the macula.

**Autosomal Dominant Vitreoretinochoroidopathy (ADVIRC)**

ADVIRC is characterized by a peripheral circumferential retinal band of pigmentary alterations, fibrillary vitreous condensations, punctate white pre or intraretinal deposits, and midperipheral and peripapillary chorioretinal atrophy. Most individuals with ADVIRC retain a fairly good visual acuity throughout life. Additional features include congenital or early-onset cataracts, microcornea, hypermetropic, and shallow anterior chamber.

**Autosomal Recessive Bestrophinopathy (ARB)**

Two pathogenic variants in BEST1 cause the clinically distinct autosomal recessive ARB, which is characterized by central visual loss and hyperopia. The age of onset ranges from 4 to 40 years of age with the average being in the 20s.

Other rare clinical presentations associated with pathogenic variants in BEST1 have also been described.

**References:**

- GeneReviews
- OMIM #607852: BEST1 gene

**Genes**

**BEST1**

**Indications**

This test is indicated for:

- Confirmation of a clinical diagnosis of a BEST1-related disorder in an individual in whom sequence analysis was negative.
- Carrier testing in adults with a family history of a BEST1-related disorder in whom sequence analysis was negative.

**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

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Specimen Collection and Shipping:
Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not 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
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 BEST1 gene is available and is required before deletion/duplication analysis.
- Several comprehensive next generation sequencing Eye Disorder Panels are available.
- 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.