Condition Description

Retinoblastoma (RB) is rare malignant tumor of the retina that occurs primarily in infancy and childhood. Approximately 60% of affected individuals have unilateral RB (affecting one eye) while the remaining 40% have bilateral RB (affecting both eyes). RB typically presents in the first five years of life; unilateral RB typically occurs at an average age of 24 months and bilateral RB typically occurs at an average age of 15 months. Retinoblastoma occurs in both hereditary and non-hereditary forms. Virtually all bilateral RB and multifocal RB as well as 15% of unilateral RB is hereditary. It is estimated that about 55% of all retinoblastoma is hereditary.

Hereditary RB is inherited in an autosomal dominant manner. Hereditary RB is caused by mutations in the tumor-suppressor gene RB1 located at 13q14.2. Individuals with hereditary RB are said to have a germline mutation in RB1. In the majority of hereditary cases, this occurs as a de novo event, however in about 20% of hereditary cases, affected individuals inherit a mutation in RB1 from a parent. In 90-95% of these patients an RB1 mutation can be detected in their blood. Individuals with a RB1 mutation have a predisposition to developing RB and other cancers, such as osteosarcomas and pinealoma.

For patients with suspected RB, 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:
- GeneReview
- Aerts I et al. Retinoblastoma. Orphanet J Rare Diseases. 2006;1:31
- OMIM #614041: RB1 gene
- OMIM #180200: RB

Genes

RB1

Indications

This test is indicated for:
- Confirmation of a clinical diagnosis of retinoblastoma in an individual 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.

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

16% of mutations can be identified by deletion/duplication analysis. 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) 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.

**Special Instructions**

Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of Emory Genetics Laboratory, please submit a copy of the sequencing report with the test requisition.

**Related Tests**

- Sequence analysis of the RB1 gene is available and is required before deletion/duplication analysis.
- 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.

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