Rothmund-Thomson Syndrome: *RECQL4* Gene Deletion/Duplication

**Test Code:** RH  
**Turnaround time:** 2 weeks  
**CPT Codes:** 81228 x1

**Condition Description**

*RECQL4*-related disorders result from mutations in the *RECQL4* gene (8q24.3) and include Rothmund-Thomson syndrome (RTS), Baller-Gerold syndrome (BGS), and Rapadilino syndrome.

Features of RTS include:

- sparse hair, eyelashes, and/or eyebrows  
- poikiloderma  
- skeletal and dental abnormalities  
- small stature  
- cataracts  
- predisposition to cancer, especially osteosarcoma [1].

BGS is characterized by:

- premature fusion of certain skull bones (craniosynostosis)  
- bulging eyes with shallow eye sockets (ocular proptosis)  
- widely spaced eyes (hypertelorism)  
- oligodactyly (reduction in number of digits)  
- aplasia/hypoplasia of the thumb and/or radius  
- poikiloderma (abnormal skin pigmentation)  
- growth retardation [2]

Rapadilino syndrome is an acronym for:

- RADial ray defect  
- PAtellae hypoplasia/aplasia and cleft/highly arched PAlate  
- DIarrhea and DIlocated joints  
- LIttle size and/or LMb malformation  
- slender NOse  
- NOrmal intelligence

Clinical examinations are the primary method for diagnosis of *RECQL4*-related disorders.

Sequencing of the *RECQL4* gene is recommended to help confirm the presence of mutations in a proband, identify at-risk individuals among the proband's relatives, and provide prenatal diagnosis in families with known mutations. Approximately 66% of individuals with a clinical diagnosis of RTS will have *RECQL4* mutations. Close to 100% of *RECQL4* mutations associated with BGS have been found in fewer than ten families. All *RECQL4*-related disorders are inherited in an autosomal recessive manner. The *RECQL4* gene (8q24.3) has 21 exons and appears to play a role in DNA repair.

For patients with suspected RTS or a *RECQL4*-related disorder, 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.

Please click here for the GeneTests summary on RTS, and here for the GeneTests summary on BGS.

**References:**


**Genes**

*RECQL4*

**Indications**

This test is indicated for:

- Mutation identification in an individual with a clinical diagnosis of a *RECQL4*-related disorder but in whom sequence analysis was negative.
- Individuals at risk for a *RECQL4*-related disorder due to family history but in whom sequence analysis was negative.

**Methodology**

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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 frequency of deletion/duplication mutations in *RECQL4*-related disorders is unknown. 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 presentation and family history.

**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**

Please submit copies of family pedigree information along with the sample. 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**

- *RECQL4* sequencing analysis is required before deletion/duplication analysis.

Due to technical issues, sequence analysis for *RECQL4* is temporarily not being offered at EGL. Deletion/duplication analysis is still available. Please check back at a later date for *RECQL4* sequence analysis availability, or call the lab for more information.

- Prenatal testing is available to couples who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.