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  
- poikilodermia  
- 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  
- poikilodermia (abnormal skin pigmentation)  
- growth retardation [2]

Rapadilino syndrome is an acronym for:
- radial ray defect  
- patellae hypoplasia/aplasia and cleft/highly arched pata  
- diarrhoea and dislocated joints  
- little size and/or limb 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**
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 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

**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

**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**

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.