Rubinstein-Taybi Syndrome: CREBBP Gene Deletion/Duplication

**Condition Description**

Rubinstein-Taybi syndrome (RSTS) is characterized by clinical findings that include broad thumbs and great toes, distinctive facial features, moderate to severe intellectual disability, and short stature. The characteristic facial features include beaked nose, grimacing smile, high arched palate, downslanting palpebral fissures, and talon cusps. Other variable features include congenital heart defects, renal abnormalities, cataract, cryptorchidism, and coloboma.

The CREBBP and EP300 genes are the only two genes known to cause RSTS. Mutations in the CREBBP gene (16p13.3) are identified in 30-50% of individuals with RSTS. Mutations in the EP300 gene are identified in 3% of individuals with RSTS. Microdeletions account for approximately 10% of individuals with RSTS. RSTS is inherited in an autosomal dominant pattern; however, most of the mutations are de novo.

Please note that this test is for the CREBBP gene only.

For patients with suspected RSTS, 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 #600140: CREBBP gene
- OMIM #180849: RSTS

**Genes**

CREBBP

**Indications**

This test is indicated for:
- Confirmation of a clinical diagnosis of Rubinstein-Taybi syndrome in an individual in whom sequence analysis was negative.
- Carrier testing in adults with a family history of Rubinstein-Taybi syndrome 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**

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:

Oragenê™ 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 EGL Genetics, please submit a copy of the sequencing report with the test requisition.

**Related Tests**

- Sequence analysis of the *CREBBP* gene is available and is required before deletion/duplication analysis.
- Sequence analysis of the *EP300* gene is 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.