Rubinstein-Taybi Syndrome: \textit{EP300} Gene Sequencing

\textbf{Test Code: SEP30}

\textbf{Turnaround time: 6 weeks}

\textbf{CPT Codes: 81479 x1}

\textbf{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 \textit{CREBBP} and \textit{EP300} genes are the only two genes known to cause RSTS. Mutations in the \textit{CREBBP} gene are identified in 30-50\% of individuals with RSTS. Mutations in the \textit{EP300} gene (22q13) 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 \textit{EP300} gene only.

\textbf{References:}

- GeneReviews
- OMIM \#602700: \textit{EP300} gene
- OMIM \#180849: RSTS

\section*{Genes}

\textit{EP300}

\section*{Indications}

This test is indicated for:

\begin{itemize}
  \item Confirmation of a clinical diagnosis of Rubinstein-Taybi syndrome.
  \item Carrier testing in adults with a family history of Rubinstein-Taybi syndrome.
\end{itemize}

\section*{Methodology}

\textbf{Next Generation Sequencing:} In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

\section*{Detection}

Clinical Sensitivity: 3\%. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical and/or biochemical phenotype.

Analytical Sensitivity: ~99\%

\section*{Specimen Requirements}

Submit only 1 of the following specimen types

\begin{itemize}
  \item Preferred specimen type: Whole Blood
\end{itemize}

\textbf{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.

\textbf{Type: Saliva}


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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.

**Related Tests**

- Sequence and deletion/duplication analysis for the **CREBBP** gene 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.