Kabuki Syndrome: KMT2D Gene Sequencing

Test Code: SML2  
Turnaround time: 4 weeks  
CPT Codes: 81479 x1

**Condition Description**

Kabuki syndrome is a rare condition that affects multiple organ systems. It is characterized by 5 cardinal features: 1) characteristic facies, (2) skeletal anomalies, (3) dermatolyphic abnormalities, (4) mild to moderate intellectual disability, and (5) postnatal growth deficiency. Additional manifestations include a broad and depressed nasal tip, large prominent earlobes, a cleft or high-arched palate, immunological defects, such as recurrent ear infections in infancy, and cardiac anomalies. The estimated prevalence is 1 in 32,000 with 400 cases reported worldwide. The majority of cases are de novo; however, parent-to-child transmission has been described.

Mutations in KMT2D, also known as MLL2, can cause Kabuki syndrome. Ng et al. reports loss-of-function mutations in 9 of the 10 individuals in their discovery population with Kabuki syndrome.


**References:**
- OMIM #147920: Kabuki Syndrome

**Genes**

KMT2D, MLL2

**Indications**

This test is indicated for:
- Confirmation of a clinical diagnosis of Kabuki syndrome.
- Carrier testing in adults with a family history of Kabuki syndrome.

**Methodology**

**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.

**Detection**

Clinical Sensitivity: Unknown. 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 biochemical phenotype.

Analytical Sensitivity: ~99%

**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.

### Related Tests

- Deletion/duplication analysis of the KMT2D gene by CGH array is available for those individuals in whom sequence analysis is negative.
- 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.