### Condition Description

Kabuki syndrome is a rare condition that affects multiple organ systems. It is characterized by five 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.

Pathogenic variants in the *KMT2D* (formerly *MLL2*) (12q13.12) or *KDM6A* (Xp11.3) gene cause Kabuki syndrome. Ng et al. reports loss-of-function mutations in *KMT2D* in 9 of the 10 individuals in their discovery population with Kabuki syndrome. *KMT2D*-related Kabuki syndrome is inherited in an autosomal dominant manner. A small number of cases of Kabuki syndrome caused by pathogenic variants in *KDM6A* have been described. All pathogenic variants reported in the *KDM6A* gene have apparently been de novo; however, X-linked inheritance is possible.


### References:

- [GeneReviews](http://www.GeneReviews.org)
- Ng et al. (2010). Nat Genet, 42(9): 790-794.

### Genes

- **KDM6A**, **KMT2D**

### 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

Next Generation Sequencing: 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/duplications will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical/biochemical phenotype. Analytical Sensitivity: ~99%.

### Specimen Requirements

**Submit only 1 of the following specimen types**

**Type**: Saliva

**Specimen Requirements**: Oragene™ Saliva Collection Kit

Oragene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.
Specimen Collection and Shipping:
Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

Type: DNA, Isolated

Specimen Requirements:
Microtainer
8µg
Isolation using the Perkin Elmer™Chemagen™ 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.

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.

Related Tests

- Sequencing and deletion/duplication analysis by CGH array of the KMT2D (formerly MLL2) and KDM6A genes individually is available.
- Kabuki Syndrome: KMT2D and KDM6A Deletion/Duplication Panel.
- 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.