Kabuki Syndrome: *KDM6A* Gene Sequencing

**Test Code:** SKDM6  
**Turnaround time:** 6 weeks  
**CPT Codes:** 81479 x1

### 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.

Please note that this test is for the *KDM6A* gene only.


### References:

- GeneReviews  
- Ng et al. (2010). Nat Genet, 42(9): 790-794.

### Genes

*KDM6A*

### 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

PCR amplification of 29 exons contained in the *KDM6A* gene is performed on the patient's genomic DNA. Direct sequencing of amplification products is performed in both forward and reverse directions, using automated fluorescence dideoxy sequencing methods. The patient's gene sequences are then compared to a normal reference sequence. Sequence variations are classified as mutations, benign variants unrelated to disease, or variations of unknown clinical significance. Variants of unknown clinical significance may require further studies of the patient and/or family members. This assay does not interrogate the promoter region, deep intronic regions, or other regulatory elements, and does not detect large deletions.

### 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 clinical and/or biochemical phenotype.

Analytical Sensitivity: ~99%

### Specimen Requirements

**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: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight delivery.
Type: Saliva

Specimen Requirements:

OrageneTM Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

Special Instructions

Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of Emory Genetics Laboratory, please submit a copy of the sequencing report with the test requisition.

Related Tests

- Deletion/duplication analysis of the KDM6A gene by CGH array is available for those individuals in whom sequence analysis is negative.
- Sequencing and deletion/duplication analysis of the KMT2D gene (formerly MLL2) is available.
- A Kabuki syndrome panel including sequencing and deletion/duplication analysis of the KMT2D and KDM6A genes is also 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.