Kabuki Syndrome: **KDM6A** Gene Deletion/Duplication

**Test Code:** DKDM6  
**Turnaround time:** 2 weeks  
**CPT Codes:** 81228 x1

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**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 in an individual in whom sequence analysis was negative.
- Carrier testing in adults with a family history of Kabuki 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**

**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: 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 EGL Genetics, please submit a copy of the sequencing report with the test requisition.

**Related Tests**

- Sequence analysis of the *KDM6A* gene is available and is required before deletion/duplication analysis.
- 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.