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

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

### 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

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

**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.

**Type: DNA, Isolated**
Specimen Requirements:
Microtainer
3µg
Isolation using the Perkin Elmer™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.

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.