Kabuki Syndrome: **KMT2D** and **KDM6A** Deletion/Duplication Panel

**Test Code:** DKABP  
**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.


**References:**

- GeneReviews  
- 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**

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**

Submit only 1 of the following specimen types

**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:

Oragene™ 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.

**Type: Isolated DNA**

Specimen Requirements:

In microtainer: 10 ug

Isolation using the Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping: Refrigerate until time of shipment in 100 ng/ul of TE buffer. Ship sample at room temperature with overnight delivery.

**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 Sequencing 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.