Oral-Facial-Digital Syndrome: *OFD1* Gene Deletion/Duplication

**Test Code:** DOFD1  
**Turnaround time:** 2 weeks  
**CPT Codes:** 81228 x1

### Condition Description

Mutations in the *OFD1* gene (Xp22.3-p22.2) can result in one of three X-linked conditions: orofaciodigital syndrome 1, Simpson-Golabi-Beahmel syndrome type 2 or Joubert syndrome 10.

**Orofaciodigital Syndrome Type 1**

Orofaciodigital syndrome type 1 (OFD1) is characterized by malformations of the face, oral cavity, and digits. Additional characteristics include thickened alveolar ridges and abnormal dentition. In up to 40% of cases, the central nervous system may be involved. About half of individuals with OFD1 will have some degree of intellectual disability, which is usually mild. Clinical features may overlap those reported in other forms of orofaciodigital syndrome, but type 1 can be distinguished by the X-linked inheritance pattern and polycystic kidney disease. It is lethal in males. 80% of mutations can be detected through sequence analysis and 5% of mutations can be found through deletion/duplication analysis. 75% of cases occur de novo.

**Simpson-Golabi-Beahmel Syndrome Type 2**

Mutations in the *OFD1* gene have been reported in families with Simpson-Golabi-Beahmel syndrome type 2. The liveborn males were hydropic at birth and had a combination of craniofacial anomalies that included macrocephaly, low-set posteriorly angulated ears, hypertelorism, short, broad nose with anteverted nares, large mouth with a thin vermilion upper border, prominent philtrum, and high-arched or cleft palate. Other features included short neck, redundant skin, hypoplastic nails, skeletal defects, gastrointestinal and genitourinary anomalies and neurological impairment.

**Joubert Syndrome 10**

Joubert syndrome is characterized by a specific hindbrain formation, hypotonia, cerebellar ataxia, dysregulated breathing patterns, and developmental delay. Mutations in multiple genes can cause Joubert syndrome; X-linked Joubert syndrome is caused by mutations in the *OFD1* gene. Other features of Joubert syndrome 10 include recurrent infections, postaxial polydactyly and juvenile-onset retinitis pigmentosa. Obligate female carriers are unaffected.

For patients with suspected Oral-Facial-Digital syndrome, sequence analysis is recommended as the first step in mutation identification. For patients in whom mutations are not identified by full gene sequencing, deletion/duplication analysis is appropriate.

### References

- OMIM #311200: Orofaciodigital Syndrome I.  
- OMIM #300170: Chromosome X Open Reading Frame 5.

### Genes

**OFD1**

### Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of Oral-Facial-Digital syndrome in an individual in whom sequence analysis was negative.  
- Carrier testing in adults with a family history of Oral-Facial-Digital 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.
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 24 hours of collection. Do not refrigerate or freeze.

**Type: DNA, Isolated**

**Specimen Requirements:**
Microtainer
3 µg
Isolation using the PerkinElmer™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**
Submit copies of diagnostic biochemical test results with the sample, if appropriate. Contact the laboratory if further information is needed.

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 *OFD1* gene is available and is required before deletion/duplication analysis.
- 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.