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

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

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**Condition Description**

Mutations in the **OFD1** gene (Xp22.3-p22.2) can result in one of three X-linked conditions: orofaciiodigital syndrome 1, Simpson-Golabi-Behekel 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 orofaciiodigital 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-Behekel Syndrome Type 2**  
Mutations in the **OFD1** gene have been reported in families with Simpson-Golabi-Behekel 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 antverted nares, large mouth with a thin vermilion upper border, prominent philtrum, and high-arched or cleft palate. Other features included short neck, redundant skin, hypoplasic 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 #300209: Simpson-Golabi-Behekel Syndrome, Type 2.  
- OMIM #300170: Chromosome X Open Reading Frame 5.  
- GeneReviews

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**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.

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.

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Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

**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: Refrigerate until time of shipment. 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: Store sample at room temperature. Ship sample within 5 days of collection 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.