

Focal Dermal Hypoplasia: *PORCN* Gene Sequencing

Test Code: SPORC

Turnaround time: 6 weeks

CPT Codes: 81479 x1

Condition Description

Intellectual disability (ID) is a nonprogressive cognitive impairment affecting 1-3% of the Western population. It is estimated that up to 50% of moderate-severe cases have genetic causes and approximately 10% are due to X-linked intellectual disability disorders (XLID). XLID can be syndromic or nonsyndromic and is observed in all ethnic groups. More than 100 XLID syndromes have been described in the literature to date. Fragile X is the most common XLID syndrome (~1 in 4000 males) while others can be quite rare with only a few patients reported in the literature. Males can have moderate to severe intellectual disability depending on the syndrome, and carrier females can also be affected, but typically have milder clinical symptoms.

Focal dermal hypoplasia is a multisystem disorder that involves the skin, skeletal system, eyes, and face. At birth, the skin manifestations present include atrophic and hypoplastic areas of skin; cutis aplasia; fat nodules in the dermis manifesting as soft, yellow-pink cutaneous nodules; and pigmentary changes. Later, verrucoid papillomas of the skin and mucous membranes may appear. The nails can be ridged, dysplastic, or hypoplastic. Hair can be sparse or absent. Skeletal findings can include oligodactyly and/or syndactyly in one or both hands or feet and split hand/foot malformations. The central digits are most often involved. A skeletal survey may help detect the presence of osteopathia striata and/or costovertebral segmentation abnormalities. The developmental abnormalities of the eyes are usually evident at birth. Depending on the severity of the abnormality, vision can range from normal to blindness. Specific eye abnormalities reported include anophthalmia/microphthalmia, microcornea, iris and chorioretinal coloboma, lacrimal duct abnormalities, and cataracts. Craniofacial findings include facial asymmetry, pointed chin, small underfolded pinnae and notched alae nasi. These features typically develop as the individual ages. Additional features include cleft lip and/or palate, dental abnormalities, gastrointestinal anomalies, such as abdominal wall defects or diaphragmatic hernia, and renal abnormalities. Development is typically normal; however, some individuals with focal dermal hypoplasia have intellectual disability.

Focal dermal hypoplasia is caused by mutations in the *PORCN* gene (Xp11.23). Affected females are heterozygous for a mutation in the *PORCN* gene or have somatic mosaicism for a *PORCN* mutation and account for 90% of cases. Affected males have somatic mosaicism for *PORCN* mutations and account for 10% of cases. It is thought that non-mosaic hemizygous males are not viable. Affected males typically have a less severe phenotype than females. Female mutations in the *PORCN* gene are approximately 95% de novo.

References:

- GeneReviews
- [OMIM #300651](#): *PORCN* gene
- [OMIM #305600](#): Focal dermal hypoplasia

Genes

[PORCN](#)

Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of Focal Dermal Hypoplasia.
- Carrier testing in adults with a family history of Focal Dermal Hypoplasia.

Methodology

PCR amplification of 14 exons contained in the *PORCN* gene is performed on the patient's genomic DNA. Direct sequencing of amplification products is performed in both forward and reverse directions, using automated fluorescence dideoxy sequencing methods. The patient's gene sequences are then compared to a normal reference sequence. Sequence variations are classified as mutations, benign variants unrelated to disease, or variations of unknown clinical significance. Variants of unknown clinical significance may require further studies of the patient and/or family members. This assay does not interrogate the promoter region, deep intronic regions, or other regulatory elements, and does not detect large deletions.

Detection

Clinical Sensitivity: Unknown. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical and/or biochemical phenotype.

Analytical Sensitivity: ~99%

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

8µg

Isolation using the Perkin Elmer™ Chemagen™ 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.

Type: Saliva**Specimen Requirements:**

Oragene™ Saliva Collection Kit

Oragene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

Specimen Collection and Shipping:

Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

Related Tests

- Deletion/duplication analysis of the *PORCN* gene by CGH array is available for those individuals in whom sequence analysis is negative.
- 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.
- X-Linked Intellectual Disability panels are available for 30, 60, and 90+ genes.