

Jalili Syndrome: *CNNM4* Gene Sequencing

Test Code: SCNNM

Turnaround time: 6 weeks

CPT Codes: 81479 x1

Condition Description

Jalili syndrome is an autosomal recessive condition characterized by visual impairment and amelogenesis imperfecta (abnormal enamel). In families with Jalili syndrome, all affected individuals had significant visual impairment, starting in infancy or early childhood and progressing with age, and abnormal enamel of the primary and secondary dentitions and were susceptible to rapid posteruptive failure due to hypomineralization. The first clinical sign of visual impairment is often nystagmus. Photophobia and achromatopsia are also present in individuals with Jalili syndrome. Pathogenic variants in the *CNNM4* gene (2q11.2) cause Jalili syndrome.

For patients with suspected Jalili syndrome, sequence analysis is recommended as the first step in pathogenic variant identification. For patients in whom pathogenic variants are not identified by full gene sequencing, deletion/duplication analysis is appropriate.

References:

- OMIM #607805: *CNNM4* gene
- OMIM #217080: Jalili syndrome
- Doucette et al. (2013), *Ophthalmic Genet*, 34:19-29.
- Parry et al. (2009), *Am J Hum Genet*, 84:266-273.

Genes

[CNNM4](#)

Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of Jalili syndrome.
- Carrier testing in adults with a family history of Jalili syndrome.

Methodology

PCR amplification of 7 exons contained in the *CNNM4* 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. Pathogenic variants in the promoter region, some pathogenic variants in the introns and other regulatory element pathogenic variants 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: 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.

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.

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

- Deletion/duplication analysis of the *CNNM4* 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.